[COMMITTEE PRINT]

ISSUES IN THE FEDERAL REGULATION OF BIOTECHNOLOGY: FROM RESEARCH TO RELEASE

REPORT

PREPARED BY THE

SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT

TRANSMITTED TO THE

COMMITTEE ON SCIENCE AND TECHNOLOGY HOUSE OF REPRESENTATIVES

NINETY-NINTH CONGRESS

SECOND SESSION

Serial X

DECEMBER 1986

Printed for the use of the Committee on Science and Technology

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U.S. GOVERNMENT PRINTING OFFICE

WASHINGTON : 1986

For sale by the Superintendent of Documents, Congressional Sales Office
U.S. Government Printing Office, Washington, DC 20402

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LETTER OF TRANSMITTAL

HOUSE OF REPRESENTATIVES,
COMMITTEE ON SCIENCE AND TECHNOLOGY,
Washington, DC, October 10, 1986.

Hon. DON FUQUA,
Chairman, Committee on Science and Technology,
House of Representatives, Washington, DC.

DEAR MR. CHAIRMAN: Enclosed is the final version of the report, "Issues in the Federal Regulation of Biotechnology: From Research to Release".

We request that the report be laid before the Committee for consideration at the earliest convenient time.

Sincerely,

HAROLD L. VOLKMER,
Chairman, Subcommittee on
Investigations and Oversight.

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PART I

INTRODUCTION

Biotechnology [1] has the promise to provide the United States and the world a wealth of organisms genetically-engineered to fight disease, clean-up pollution, enhance food production, and decrease the use of harmful chemicals. The capacity of modern genetic engineering to introduce completely new traits into existing organisms has given rise to a new industry of over 200 companies in the United States alone.[2] The Committee on Science and Technology has long been involved in promoting the development of a safe biotechnology industry. This report continues that involvement by examining current issues in the regulation of environmental releases of genetically-engineered organisms.

On May 30, 1986, the first authorized release of a genetically-engineered organism occurred in Middleton, Wisconsin, when Agracetus Corporation planted 200 tobacco plant seedlings that had been genetically-altered to be resistant to a specific disease.[3] However, this first *authorized* release may not have been the first *actual* release. In June of 1984, scientists in Texas inoculated a herd of swine with a live genetically-engineered vaccine in order to prevent an outbreak of pseudorabies, a disease often fatal to cattle and swine.[4] The shedding of the genetically-engineered virus in the test animals' body fluids may have constituted an environmental release of the vaccine's virus. A few months later in January of 1985, scientists at Advanced Genetic Sciences, Inc. in California injected a live genetically-engineered bacteria into fruit trees located in the open air on the roof of their building.[5] The trees bled sap that may have contained the genetically-engineered bacteria.

These three events come at the beginning of a new chapter in biotechnology—the development of live, genetically-engineered organisms that are intended to be used uncontained in the environ-

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[1] "Biotechnology" has been defined in various ways. For the purpose of this report, biotechnology is, "(t)he process of *in vitro* alteration of genetic material for the purpose of creating new gene combinations or modifications." *The U.S. Department of Agriculture's Biotechnology Research Efforts,* General Accounting Office, #GAO/RCED-86-39BR, October 1985, at 9. (Hereinafter cited as "USDA's Biotechnology Research"). This definition implies that biotechnology is, "(a)ny technique that uses living organisms (or parts of organisms) to make or modify products, to improve plants or animals or to develop microorganisms for specific uses." *Commercial Biotechnology: An International Analysis,* United States Congress, Office of Technology Assessment, Washington, DC; Government Printing Office OTA-BA-218, 1984. (Hereinafter cited as "Commercial Biotechnology".)

[2] Olson, S., *Biotechnology: An Industry Comes of Age,* National Academy Press, Washington, DC, 1986 at 3.

[3] *New York Times,* May 30, 1986. "Gene-Altered Tobacco is Planted in Wisconsin". The disease was Crown Gall.

[4] *See* discussion, *infra,* Part II, Chapter Three.

[5] *See* discussion, *infra,* Part II, Chapter Two.

ment. As this new chapter unfolds, a federal regulatory system for biotechnology is unfolding as well.

The Federal regulation of biotechnology is now in its third stage. The first stage began with the "Guidelines for Research Involving Recombinant DNA Molecules". ("NIH Guidelines") adopted by the National Institutes of Health (NIH) in 1976.[6] These guidelines took a cautious stance, emphasizing containment standards and preliminary review by committees at each research institute of proposed experiments involving recombinant DNA technology. The guidelines have been gradually relaxed as scientists obtained more information about the safety of the organisms involved.[7]

The second stage of biotechnology regulation began on December 31, 1984, when the Office of Science and Technology Policy (OSTP) published a "Proposal for a Coordinated Framework for Regulation of Biotechnology." [8] The purpose of the proposal was to "provide a concise index of U.S. laws related to biotechnology, to clarify the policies of the major regulatory agencies that will be involved in reviewing research and products of biotechnology, to describe a scientific advisory mechanism for assessment of biotechnology issues, and to explain how the activities of the federal agencies in biotechnology will be coordinated." [9]

The Proposed Coordinated Framework served as guidelines for the review of biotechnology products until June 26, 1986, when the Office of Science and Technology Policy published the "Coordinated Framework for Regulation of Biotechnology." [10] This "Coordinated Framework" incorporated the comments received on the December 1984 Proposed Coordinated Framework and contained revised and expanded agency policy statements regarding the regulation of biotechnology products. This began the third and present stage of government regulation of biotechnology. Although nearly a score of bills specifically designed to regulate biotechnology have been introduced in the House and Senate in the past 16 years, none have become law.

From December 1985 through July 1986, the Investigations and Oversight Subcommittee of the House Committee on Science and Technology held a series of hearings which, taken as a whole, chronicle the journey from the NIH Guidelines to the Coordinated Framework. The first hearing, which was held one year after the publication of the Proposed Coordinated Framework, examined the status of government research into, and regulation of, planned releases of genetically-engineered organisms.[11] The next two hearings investigated review and regulation under the Proposed Coordinated Framework of two genetically-engineered products, "ice-

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[6] 41 Fed. Reg. 131, Part II, at 27902-27943, July 7, 1976. (Hereinafter cited as "NIH Guidelines".)

[7] The most recent revision is found in 51 Fed. Reg. 16958, May 7, 1986.

[8] 49 Fed. Reg. 252, Monday, December 31, 1984, at 50856-50907. (Hereinafter cited as "Proposed Coordinated Framework".)

[9] *Id.*, at 50856.

[10] 51 Fed. Reg. 123, Thursday, June 26, 1986, at 23302-23393. (Hereinafter cited as "Coordinated Framework".)

[11] "Planned Releases of Genetically-Altered Organisms: The Status of Government Research and Regulation", Hearing before the Subcommittee on Investigations and Oversight of the Committee on Science and Technology, U.S. House of Representatives, 99th Congress, First Session, December 4, 1985, Serial No. 99-72. (Hereinafter cited as "Hearing: Planned Releases".)

minus" bacterial [12] and the pseudorables vaccine, "OMNIVAC".[13] These specific events provide a view of the operation of the December 1984 Proposed Coordinated Framework and expose the problems that any successful guidelines must address. Finally, on July 23, 1986, the Subcommittee held a hearing on the Administration's Coordinated Framework for Regulation of Biotechnology.[14]

A lawsuit challenging the Coordinated Framework was filed in the United States District Court for the District of Columbia shortly after the Coordinated Framework was published. The plaintiffs allege that the federal defendants violated the National Environmental Policy Act and the Administrative Procedures Act in developing the Coordinated Framework. None of the discussion of the Coordinated Framework contained herein is intended to respond to, relate to, or in any way comment on the issues raised in the suit. This report focuses exclusively on issues before the Investigations and Oversight Subcommittee. Accordingly, the discussions, findings, and recommendations in this report should be treated as a contribution to the ongoing dialogue on the issues biotechnology presents.

This report is divided into four parts. Part one provides general background for the issues examined in the Investigations and Oversight Subcommittee's four hearings. It details recent developments in the biotechnology industry, describes the general nature of the NIH Guidelines, the December 1984 Proposed Coordinated Framework, and the June 26, 1986 Coordinated Framework, and summarizes Congress' concerns about biotechnology from the early days of genetic engineering to the present.

Part two presents detailed discussion of the Subcommittee's hearings related to the Proposed Coordinated Framework. This encompasses the December 4, 1985 hearing on the status of biotechnology research and regulation, the March 4, 1986 hearing on Advanced Genetic Sciences', Inc. rooftop experiment with ice-minus, and the April 29, 1986 hearing on USDA's licensing of a pseudorabies vaccine.

Part three examines the Subcommittee's hearing on the June 1986 Coordinated Framework and discusses the questions and problems raised by that Framework.

Part four presents the Subcommittee's findings and recommendations from these hearings.

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[12] " 'Ice-Minus': A Case Study of EPA's Review of Genetically-Engineered Microbial Pesticides", Hearing before the Subcommittee on Investigations and Oversight of the Committee on Science and Technology, U.S. House of Representatives, 99th Congress, Second Session, March 4, 1986, Serial No. 99-117 (Hereinafter cited as "Hearing: Ice-Minus".)

[13] "USDA Licensing of a Genetically Altered Veterinary Vaccine", Joint Hearing before the Subcommittee on Investigations and Oversight of the Committee on Science and Technology and the Subcommittee on Department Operations, Research, and Foreign Agriculture of the Committee on Agriculture, U.S. House of Representatives, 99th Congress, Second Session, April 29, 1986, Serial No. 99-115. (Hereinafter cited as "Hearing: USDA Licensing".)

[14] "Coordinated Framework for Regulation of Biotechnology", Joint Hearing before the Investigations and Oversight Subcommittee; Natural Resources, Agriculture Research and Environment Subcommittee; and the Science, Research and Technology Subcommittee of the Committee on Science and Technology, U.S. House of Representatives, 99th Congress, Second Session, July 23, 1986. (Hereinafter cited as "Hearing: Coordinated Framework").

CHAPTER ONE: INDUSTRIAL DEVELOPMENT

Product development in the biotechnology industry is proceeding at an accelerating rate of speed. In 1981, the Recombinant DNA Advisory Committee (RAC) of NIH approved a genetically-engineered corn plant for use in the environment.[15] In 1983, the RAC approved two additional field tests—one involving recombinant DNA-derived tomato and tobacco plants and one involving "ice-minus", a microbe which inhibits frost formation.[16] That same year the RAC refused to approve two other proposals for environmental releases of genetically-engineered organisms.[17]

In 1984, there was another increase in the number and diversity of proposals submitted to the government to release genetically-engineered organisms into the environment. These proposals included organisms ranging from plants genetically-engineered to be herbicide- or disease-resistant, to genetically-engineered micobial pesticides. In the same year, a genetically-engineered live virus vaccine was tested on almost 1,400 swine in West Texas.

By 1985, there was, at both the Environmental Protection Agency (EPA) and the U.S. Department of Agriculture (USDA), a backlog of proposals to release genetically-engineered organisms into the environment. Also in that year, a GAO study revealed that USDA was funding at least 87 projects involving the environmental release of gentically-engineered organisms; the majority of these releases would occur in the next five years.[18]

In 1986, several types of genetically-engineered plants have actually been planted in outdoor test plots around the country.[19] This increase in field tests can be expected to continue as many more products move from the lab to the field.[20]

The expectations for future applications of biotechnology are enormous both here and in other countries. While the United States is viewed as the world's leader in biotechnology research, other countries have active and growing programs. The most advanced are those in Japan, the Federal Republic of Germany, the United Kingdom, Switzerland, and France.[21] In order for the United States to maintain a competitive edge in both research and commercial development, it will be necessary to balance the need

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[15] "The Environmental Implications of Genetic Engineering" Staff Report, Prepared by the Subcommittee on Investigations and Oversight, Transmitted to the Committee on Science and Technology, U.S. House of Representatives, 98th Congress, Second Session, Serial V, February 1984, at 17.

[16] *Id., see also,* discussion, *infra,* Appendix A.

[17] *Id.*

[18] *See* "USDA's Biotechnology Research", *supra,* note 1.

[19] In addition to Agracetus' field test in Wisconsin, Ciba-Geigy is testing an herbicide-resistant tobacco plant in North Carolina, and Rohm & Haas is testing a pesticidal plant in Mississippi and Florida.

[20] A list of proposals submitted to USDA and EPA and the status of those proposals is provided in Appendix B, *infra.*

[21] *See* "Commercial Biotechnology", *supra,* note 1, at 3.

for strong safety and environmental regulations with the need to not be unreasonably restrictive.

The OTA report on Commercial Biotechnology was very clear on this point. It concluded, ". . . clarification and modification of certain aspects of U.S. health, safety, and environmental regulation and intellectual property law may be necessary for the maintenance of a strong U.S. competitive position in biotechnology." [22] The implication for Congress is to strive to develop a balanced approach.

Rep. Packard explored this approach with Dr. Bernadine Healy, (then) Deputy Director of the Office of Science and Technology Policy, in an April 1985 hearing on "Biotechnology and Agriculture":

> Mr. PACKARD. I'm concerned about any set of regulations as to how it will affect the private sector in terms of competition in the world market place, and I don't think our research can be excluded from this concern.
>
> Dr. HEALY. I think there's no doubt that if we don't have as a first step a clear regulatory message out there to industry that we are going to have a detrimental effect. And that's why I quoted the President's Commission on Industrial Competitiveness. Those people said it better than I. That if we don't have—*if we have regulatory chaos, that is going to be our worst enemy in terms of our economic advantage and our international competitiveness.*[23] [Emphasis added.]

Dr. Ralph Hardy, President of BioTechnica International, Inc. and Chairman of the National Research Council Committee that produced "New Direction in Bioscience and Agriculture: High Reward Opportunities" supports the conclusion reached by Dr. Healy:

> Dr. HARDY. What will be the impact of regulation? . . . In a broader sense, the United States could lose its competitive edge, as has been previously mentioned. *U.S. companies in the extreme could move abroad if regulation becomes excessive.* Delays in the prudent development or product development or costly regulatory clearances would be, I think, catastrophic for start-up companies.[24] [Emphasis added.]

There is no disagreement that the United States must maintain its position as world leader in biotechnology research and commercial development. Moreover, there is concern that that position could be jeopardized by excessive regulation. While there is little agreement as to the definition of "excessive" regulation, there is widespread agreement that regulations are necessary to protect health and the environment. The Administration's Coordinated Framework is intended to balance these concerns. This report discusses the Administration's efforts and makes recommendations that are intended to improve the regulatory process.

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[22] *Id.*, at 5.

[23] "Biotechnology and Agriculture", Hearing before the Subcommittee on Investigations and Oversight of the Committee on Science and Technology, U.S. House of Representatives, 99th Congress, First Session, April 16 and 17, 1985, Serial No. 18, at 258.

[24] *Id.*, at 167.

CHAPTER TWO: THE NIH GUIDELINES

In 1976, the NIH adopted the "Guidelines for Research Involving Recombinant DNA Molecules."[25] The NIH Guidelines establish containment standards and various degrees of review for certain categories of experiments. They also require the establishment of an Institutional Biosafety Committee (IBC) at any federally-funded institution doing recombinant DNA work. Local IBCs review research proposals for compliance with the NIH policy regarding recombinant DNA research. The NIH/RAC and the director of NIH enforce the NIH Guidelines on the national level. While there have been isolated deviations from the research guidelines,[26] the record of safety in recombinant DNA laboratory research is impressive. The NIH Guidelines are used internationally as a commendable example of self-regulation by the scientific community.

Since their inception, the NIH Guidelines have been consistently criticized for three short-comings.[27] First, they are mandatory only for federally funded research; compliance by private companies is voluntary. Second, they do not apply to organisms created by genetic engineering methods other than recombinant DNA techniques. Finally, the NIH Guidelines were not originally intended to, and in fact do not, adequately address the issue of planned releases of genetically-engineered organisms into the environment.[28] The increase in proposals for environmental releases of genetically-engineered organisms has underscored these weaknesses in the NIH Guidelines. Despite these criticisms, there is general agreement that the NIH Guidelines have successfully promoted safe laboratory research in recombinant DNA technology and have set the safety standards utilized by both public and private research institutions and companies.

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[25] 41 Fed. Reg. 27902; Previous reports of this Subcommittee and other Subcommittees have presented thorough discussions of the impetus and evolution of the NIH Guidelines for Research Involving Recombinant DNA Molecules. *See* reports cited in discussion, *infra*, at 11–13.

[26] In two incidents in the late 1970s, researchers (including one former member of the NIH/RAC) circumvented the NIH Guidelines and local IBCs failed to take appropriate actions. For a discussion of the incidents, *see*, "Genetic Engineering, Human Genetics, and Cell Biology: Evolution of Technological Issues, Biotechnology" (Supplemental Report III), Prepared for the Subcommittee on Science, Research and Technology of the Committee on Science and Technology, U.S. House of Representatives, Ninety-Sixth Congress, Second Session, by the Science Policy Research Division, Congressional Research Service, Library of Congress, August 1980, Serial DDD.

[27] *Agriculture's Regulatory System Needs Clarification*, General Accounting Office, #GAO/RCED 86–59, March 1986, at 19. (Hereinafter cited as "USDA's Regulatory System".)

[28] *Id.*

CHAPTER THREE: THE PROPOSED COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY, DECEMBER 31, 1984

In 1984, the Administration, under the auspices of the (then) White House Cabinet Council on Natural Resources and the Environment (now the Domestic Policy Council) established a Working Group on Biotechnology, which operated through the Office of Science and Technology Policy (OSTP).[29] On December 31, 1984, OSTP published the "Proposal for a Coordinated Framework for Regulation of Biotechnology".[30] The proposal indexed federal laws relating to biotechnology and contained policy statements by the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), and the U.S. Department of Agriculture (USDA) related to the regulation of biotechnology. It proposed that regulatory authority for biotechnology be consolidated under the Department of Health and Human Services (DHHS). Specifically, the proposal reduced the role NIH played in biotechnology regulation and proposed the establishment of a new, centralized advisory committee to be known as the Biotechnology Science Board.[31]

The policy statement provided by FDA, USDA, and EPA did not describe regulatory requirements "but rather the general policy framework within which regulatory decisions will be made." [32] The actual regulatory authorities upon which the agencies would rely was contained in a matrix of laws, published in the Proposed Coordinated Framework.[33]

A. FDA

In its policy statement, FDA noted its "extensive experience with the administrative and regulatory regimens described as applied to the products of biotechnological processes new and old." [34] Therefore, the agency proposed no new procedures or requirements for biotechnology products under its jurisdiction. FDA's overriding policy was that regulation must be based on a case-by-case scientific evaluation of products and not on assumptions about certain technological processes.

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[29] *See* discussion in 51 Fed. Reg. 23302.

[30] 49 Fed. Reg. 50856.

[31] *Id.*; Each agency was to have its own advisory committee which would be represented on the Biotechnology Science Board (BSB). However, after receiving primarily negative comments on the proposal, the Administration proposed instead the establishment of the Biotechnology Science Coordinating Committee (BSCC) within the Federal Coordinating Council for Science Engineering and Technology (FCCSET) under OSTP.

[32] *Id.*, at 50858.

[33] *Id.*, at 50856.

[34] *Id.*, at 50878.

B. EPA

EPA's policy statement in the Proposed Coordinated Framework addressed the regulation of genetically-engineered organisms under two separate statutes, the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA),[35] which governs pesticides, and the Toxic Substances Control Act (TSCA),[36] which governs all new chemical substances, including genetically-engineered organisms.[37]

FIFRA requires pesticide manufacturers to obtain an Experimental Use Permit (EUP) before testing or using pesticides on areas over 10 acres of land, or 1 surface acre of water.[38] EPA has adopted an "interim" policy under which an EUP is required for *all* field tests of non-indigenous and genetically-engineered microbial pesticides.[39]

Also in the Proposed Coordinated Framework, EPA re-affirmed its position that certain genetically-engineered microorganisms can be reviewed under TSCA because that statute applies to "any organic or inorganic substance of a particular molecular identity, including (i) any combination of such substances occurring in whole or in part as a result of a chemical reaction or occurring in nature . . .".[40] Under TSCA, EPA can require manufacturers of genetically-engineered organisms to submit *inter alia* premanufacturing notices for new organisms or new uses of an organism, production volume reports, and reports of significant risks posed by particular genetically-engineered organisms.[41]

C. USDA

USDA expressed its regulatory philosophy in the Proposed Coordinated Framework as follows:

> USDA anticipates that agriculture and forestry products developed by modern biotechnology will not differ fundamentally from conventional products.
>
> We believe that the existing regulatory framework of USDA combined with the NIH Guidelines which are mandatory for all research grants are adequate and appropriate for regulating research, development, testing and evaluation, production, and application, of these biotechnology products. Should any new processes or products be shown to require additional regulatory measures, USDA will amend its regulations or will request additional authority.[42]

In the area of veterinary biological products, USDA's licensing policy, similar to FDA's, is to evaluate each product on a case-by-case basis. USDA's Proposed Coordinated Framework policy statement did state that the Department, "requires all licensed applicants or products derived from DNA technology to comply with the NIH Guidelines for research involving recombinant DNA molecules."[43]

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[35] U.S.C. § 136–136Y, Pub. L. 92–516.
[36] U.S.C. § 2601–2629, Pub. L. 94–469.
[37] *See* 49 Fed. Reg. 50856 for EPA's discussion of its authority to regulate genetically-engineered organisms under TSCA.
[38] FIFRA 7 U.S.C. § 136(a).
[39] 49 Fed. Reg. 40659. October 17, 1984; The Proposed Coordinated Framework continued this policy.
[40] 49 Fed. Reg. 50856.
[41] *See* TSCA 15 U.S.C. §§ 5, 8(a) and 8(e).
[42] 49 Fed. Reg. 50856, at 50898.
[43] *Id.*, at 50900.

CHAPTER FOUR: THE COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY, JUNE 26, 1986

On June 26, 1986, the Office of Science and Technology Policy published a "Coordinated Framework for Regulation of Biotechnology" that describes the Administration's policy for the regulation of biotechnology, defines which organisms would be subject to full, and which to abbreviated review, and contains specific policy statements from FDA, EPA, USDA, NIH, and the Occupational Safety and Health Administration (OSHA).[44] The Coordinated Framework establishes a regulatory scheme for both commercial and research releases of genetically-engineered organisms. This scheme is summarized in Charts I and II in Appendix C of this report.

The Coordinated Framework was compiled by the interagency committee entitled the Biotechnology Science Coordinating Committee (BSCC) under the direction of the DPC Working Group on Biotechnology.[45] The BSCC comprises representatives from NIH, National Science Foundation (NSF), EPA, FDA, and USDA.

The charter authorizes the BSCC to:

Serve as a coordinating forum for addressing scientific problems, sharing information, developing consensus; Promote consistency in the development of federal agencies' review, procedures, and assessment; Facilitate continuing cooperation among

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[44] 51 Fed. Reg. 23302.

[45] The government-wide effort to coordinate the regulation of research involving, and products using, biotechnology was first directed by the interagency Cabinet Council Working Group on Biotechnology, who developed The Proposed Coordinated Framework for Regulation of Biotechnology. The Cabinet Council Working Group on Biotechnology, established in April 1984, included as member agencies the Departments of: Interior, Justice, State, Agriculture, Commerce, Defense, Energy, Health and Human Services, and Labor; the Environmental Protection Agency; the Council on Environmental Quality; the Council of Economic Advisors; the Office of Management and Budget; the Office of Policy Development; the National Science Foundation, the Office of the U.S. Trade Representative, and the Office of Science and Technology Policy. [49 Fed. Reg. 252 at 50857.]

This working group was succeeded by the Domestic Policy Council Working Group on Biotechnology, which was responsible for the development of the Coordinated Framework for Regulation of Biotechnology. The Domestic Policy Council Working Group on Biotechnology also considers policy matters related to biotechnology, including jurisdiction, commercialization, and international aspects. [51 Fed. Reg. 123 at 23306.] It monitors developments in biotechnology and is ready to identify problems and make appropriate recommendations for their solution. [51 Fed. Reg. 123 at 23306.]

The Domestic Policy Council Working Group on Biotechnology proposed creation of the Biotechnology Science Coordinating Committee (BSCC) as the committee responsible for coordination and consistency of scientific policy and scientific reviews. The BSCC, established October 31, 1985, as part of the Federal Coordinating Council for Science, Engineering and Technology (FCCSET) within OSTP, consists of senior policy officials involved in the oversight of biotechnology research and products. [51 Fed. Reg. 123 at 23306.] Its seven members represent the Department of Agriculture (two members), the Department of Health and Human Services, the Environmental Proteciton Agency (two members), the Food and Drug Administration, and the National Science Foundation. One of the primary activities of the BSCC has been the development of definitions essential to a coordinated Federal framework. [51 Fed. Reg. 123 at 23306.] The BSCC was also helpful in the formulation of two underlying principles of the Coordinated Framework: 1) that agencies should seek to adopt consistent definitions of those genetically-engineered organisms subject to review to the extent permitted by their respective statutory authorities, and 2) that agencies should utilize reviews of comparable rigor. [51 Fed. Reg. 123 at 22303.]

federal agencies on emerging scientific issues; and identify gaps in scientific knowledge.[46]

A. FDA

Consistent with its policy statement in the Proposed Coordinated Framework, FDA did not propose any revisions in the review of biotechnology products. FDA relies on its authority under the Federal Food, Drug and Cosmetic Act and the Public Health Services Act to regulate products regardless of how they are manufactured.[47]

B. EPA

EPA's statement in the Proposed Coordinated Framework received many critical comments expressing concern that the agency drew too direct a relationship between the technology used to create an organism and the risk presented by the organism. The Agency revised its earlier "process-based" approach[48] to give particular attention, under FIFRA and TSCA, to microorganisms that (1) are used in the environment, (2) are pathogenic or contain genetic material from pathogens, or (3) contain new combinations or traits. "EPA believes these categories have sufficiently high potential for wide-spread exposure, adverse effects, or uncertainty concerning potential effects to deserve particular regulatory scrutiny."[49]

EPA's review of microorganisms under FIFRA expands on and relaxes its interim policy. EPA has now adopted a two-level review system under which microbial pesticides that pose less risk to the environment receive an abbreviated review and may be field tested without an EUP.[50] In addition, EPA detailed in its policy statement how TSCA would be applied to genetically-engineered organisms through promulgation of new rules where necessary.[51]

C. USDA

In its policy statement, USDA reiterated its position that products developed through biotechnological methods do not differ from those developed using conventional techniques.[52] For its regulatory authority, USDA relies on the matrix of laws it published in December of 1984.[53] The policy statement also provided an Advanced Notice of Proposed Guidelines for Biotechnology Research.[54] These guidelines are patterned after the NIH Guideline and are mandatory for all USDA funded research. Voluntary compliance is anticipated for other forms of agricultural research.

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[46] *See* BSCC Charter, Appendix D, *infra.*

[47] 51 Fed. Reg. 23302; Federal Food, Drug, and Cosmetic Act, Pub. L. 91-513, 21 U.S.C. § 301; Public Health Services Act, 42 U.S.C. 201, *et. seq.*

[48] 51 Fed. Reg. 23302, at 23315.

[49] Id.; EPA's review of microorganisms applied to the environment is summarized in Appendix E, *infra.*

[50] *Id.*, at 23319.

[51] *Id.*, at 23324.

[52] 51 Fed. Reg. at 23336.

[53] 49 Fed. Reg. at 50856.

[54] 51 Fed. Reg. at 23367.

CHAPTER FIVE: CONGRESSIONAL CONCERNS

Since the advent of biotechnology, Congress has published extensive reports on the issues surrounding genetic engineering. This chapter provides a brief overview of the most significant House of Representative reports of the past 16 years, legislation that has been introduced in the 99th Congress, and reports by the General Accounting Office.

A. Genetic Engineering—Evolution of a Technological Issue

(Supplemental Report I), (1974).[55]

This report, which pre-dates the convening of the Asilomar Conference,[56] concluded that, "[i]t is no longer feasible to talk in terms of developments in the far future when considering the topic of genetic engineering . . . it now appears to be necessary to prepare for the availability of many of these techniques and to determine whether additional public policies need to be adopted." The report commended the science community for recommending deferral of potentially hazardous research pending evaluation of "the legal, moral and ethical aspects of these new developments in genetic engineering."

* * * * * * *

B. Genetic Engineering, Human Genetics, and Cell Biology—Evolution of Technological Issues—DNA Recombinant Molecule Research

(Supplemental Report II), (1976).[57]

This report concluded that the NIH Guidelines represented a compromise between those who would stop all recombinant DNA research until all of the pertinent public policy or safety questions were answered and those who would prefer to go unhindered in their research. It noted that although the NIH Guidelines provided a system of peer review starting at the level of the individual investigator, there was really no central control over all recombinant DNA research.

The report concluded that there was insufficient information available to predict whether there would be adverse environmental hazards from release of genetically-engineered organisms and that

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[55] Report prepared for the Subcommittee on Science, Research and Development of the Committee on Science and Astronautics, U.S. House of Representatives, 93rd Congress, Second Session, by the Science Policy Research Division, Congressional Research Service, Library of Congress, Serial BB, December 1974.

[56] The International Conference on Recombinant DNA Molecules held at the Asilomar Conference Center in Pacific Grove, CA, February 24-27, 1975.

[57] Report prepared by the Congressional Research Service for the Subcommittee on Science, Research and Technology of the Committee on Science and Technology, U.S. House of Representatives, 94th Congress, Second Session, Serial KKK (December 1976).

this concern had temporarily slowed progress in this field. The report noted that very little funding had been directed towards research on the environmental consequences associated with the use of these organisms.

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C. Science Policy Implications of DNA Recombinant Molecule Research, (1978)[58]

This report found that the benefits of recombinant DNA research appeared to outweigh the hypothesized risks. The report concluded that research in this area should continue to be supported and that the greatest improvement and understanding would occur when lines of communication were opened between scientists and the public.

Specifically, the report found that: (1) The burden of proof of safety factors should not be borne exclusively by proponents of the research, but also by opponents; (2) Current DNA research did not pose a significantly greater risk than natural diseases confronting the medical community of today; (3) The NIH Guidelines for Recombinant DNA Research should be extended to include non-federally funded recombinant DNA research and better legal procedures for implementing the Guidelines should be developed; (4) Procedures for public participation in revising the NIH Guidelines should be improved; (5) It was not presently possible to use traditional forms of risk benefit analysis developed for past technological research with regard to recombinant DNA research; (6) Risk-evaluation should be monitored by researchers, a formal public body, and a "National Commission" that could provide a forum for public participation; (7) Communications between scientists and the public was less then adequate, both with respect to the scientists' level of social responsibility and awareness and the public's understanding of scientific significance.

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D. Genetic Engineering, Human Genetics, and Cell Biology—Evolution of Technological Issues—Biotechnology

(Supplemental Report III), (1980).[59]

This report examined capabilities in genetics and cell biology, including related ethical and public policy issues involved with medical genetic research. This report found that although there seemed to have been a major reduction in the conflict regarding recombinant DNA research, all concern had not been alleviated. It cited concerns of industrial compliance with the NIH Guidelines and the occupational health issues.

The report recognized that this technology would have significant applications in medicine and chemistry. The report found that while these advances provided important options for resolution of

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[58] Report by the Subcommittee on Science, Research and Technology, Committee on Science and Technology, U.S. House of Representatives, 95th Congress, Second Session, Serial X, March 1978.

[59] *See* note 26, *supra.*

resource and health problems, any proposals for a new or changed role of the Federal Government in regulating or fostering innovation in these fields would depend upon continuous monitoring and evaluation of these innovations.

The report concluded that genetic engineering would have a major impact on U.S. international policies in terms of balance of trade, international competition, global conservation of resources, and other foreign policy issues.

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E. The Environmental Implications of Genetic Engineering (1984)[60]

This report concluded that:

(1) The potential environmental risks associated with the deliberate release of genetically-engineered organisms were best described as "low probability of high consequence risks"; that is, while there was only a small possibility of occurrence, the damage that could occur would be great.

(2) Predicting the specific type, magnitude or probability of environmental effects associated with deliberate release would be extremely difficult at the present time.

(3) The current regulatory framework did not guarantee that adequate consideration would be given to potential environmental effects of a deliberate release.

Based on these conclusions, the report recommended (1) enhancement of EPA's expertise and efforts in biotechnology; (2) establishment of an interagency task force to review release proposals, promote risk assessment programs and develop guidelines for releases; (3) referral by NIH to the appropriate agency of industrial requests to release biotechnology products into the environment; and (4) General Accounting Office review of USDA's efforts to promote and regulate biotechnology.

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F. Biotechnology: The U.S. Department of Agriculture's Biotechnology Research Efforts (October 1985) and Agriculture's Regulatory System Needs Clarification (March 1986), Prepared by U.S. General Accounting Office)[61]

In March 1984, the Committee on Science and Technology asked the General Accounting Office (GAO) to obtain information from the USDA in the following areas: (1) Programs and activities that relate to biotechnology; (2) Decision-making concerning the release of genetically-engineered organisms into the environment; and (3) Relationships with other federal agencies involved in biotechnology. In addition, they were asked to obtain information regarding USDA's communication of its view of biotechnology and the regulatory role USDA would play. The Committee also asked GAO to survey and report on USDA-funded research projects in biotechnology.

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[60] *See* "The Environmental Implications of Genetic Engineering", *supra,* note 15.

[61] *See* notes 1 and 27, *supra.*

GAO observed that biotechnology oversight was handled by divisions within the Department that had other regulatory and/or research responsibilities. The GAO concluded that these divisions within USDA had been struggling for regulatory control. The questions concerning jurisdiction were exacerbated by the fact that the Agriculture Recombinant DNA Research Committee—USDA's designated focal point for biotechnology—lacked authority and direction.

GAO also recommended to the Secretary of Agriculture that the Department should: (1) complete the development of a formalized, well-defined biotechnology regulatory structure that will identify USDA's regulatory path for licensing biotechnology products and approving requests involving deliberate releases; (2) provide the Agriculture Recombinant DNA Research Committee (or a future central committee within the USDA) with the authority and sense of direction it needs to act efficiently as the Department's focal point for biotechnology; and (3) look for and take advantage of opportunities to improve and increase the communication of USDA's views concerning biotechnology, both in terms of the benefits to be derived and the risks that must be considered and managed.

The section of the report dealing with USDA-funded biotechnology research projects was based on a survey administered in conjunction with the National Association of State and Land Grant Universities. The 1985 report revealed that 87 USDA-funded projects would lead to the intentional release of genetically-altered organisms into the environment. The majority of these releases may occur during the next five years (11 within 1 year, 47 within 2 to 5 years, and 29 after 5 years). Only 3 of the 87 research projects cited in the report actually incorporated broad-based risk assessment into the project design itself.[62]

G. Legislation

The Biotechnology Science Coordination Act of 1986, H.R. 4452, introduced March 19, 1986 by Representative Don Fuqua

This bill proposes to establish by statute a Biotechnology Science Coordinating Committee (BSCC), within the Office of Science and Technology Policy in the Executive Office of the President, to serve as a forum to coordinate review and assessment by the various federal agencies of information regarding genetically-engineered organisms. In addition, it proposes to establish a Biotechnology Science Research Program within the Office of Science and Technology Policy. Under this program, private industry and government agencies would jointly fund research necessary to create a data base to support the development and regulation of biotechnology. The program would be conducted under the supervision of a Board of Governors selected by the BSCC to be independent of both the government and industry participants. Finally, the bill amends the Toxic Substances Control Act and certain acts USDA administers to pro-

[62] There are a broad variety of organisms involved in these USDA-funded research projects, ranging from crop plants to animals to microbes. Each type of organism poses its own set of concerns. The scientists working on these projects generally stated that these planned releases will cause no environmental problems.

hibit the release, use or distribution of organisms genetically-engineered to contain genetic material from different genera without a permit issued by the Secretary of USDA or the Administrator of EPA, as the case may be.

The bill was referred jointly to the Committees on Science and Technology, and Energy and Commerce, and Agriculture. Joint hearings were held on the bill by the Natural Resources, Agricultural Research and Environment Subcommittee and the Science, Research and Technology Subcommittee of the Science and Technology Committee on June 4 and 5, 1986.

Biosafety Act S. 1967, introduced December 17, 1985 by Senator Durenberger and Senator Baucus

This bill would require review and approval by EPA before genetically-engineered microorganisms could be released into the environment or used in manufacturing. It defines genetically-engineered microorganisms to mean bacteria, virus, fungi, blue-green algae or protists "the genetic material of which has deliberately been altered by human intervention." The bill proposes to establish a Biotechnology Science Coordinating Committee to serve as a coordinating forum to address scientific problems related to methods for evaluating potential adverse effects caused by genetically-engineered organisms.

The bill was referred to the Committee on Environment and Public Works. No hearings have been held on the bill.

PART II

ISSUES RELATED TO PROPOSED COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY

The first wave of applications to release genetically-engineered organisms into the environment was directed to the NIH/RAC for review.[1] However, many of these early products of biotechnology were agricultural products or pesticides—products which NIH had little experience or interest in reviewing.[2] Thus, the Administration's Proposed Coordinated Framework, published in December 1984, was a welcome addition to the growing federal system for the regulation of biotechnology.

This part of the report first examines industry and government's assessment of the Proposed Coordinated Framework one year after it was published. It then presents two cases in which unauthorized environmental releases of genetically-engineered organisms may have occurred.

[1] *See,* "Environmental Implications of Genetic Engineering," *supra*, note 15, Part I.
[2] *Id.*

CHAPTER ONE: PLANNED RELEASES OF GENETICALLY-ENGINEERED ORGANISMS: THE STATUS OF GOVERNMENT RESEARCH AND REGULATION

On December 4, 1985, the Investigations and Oversight Subcommittee held a hearing to examine the Proposed Coordinated Framework for the Regulation of Biotechnology, and to learn which areas of scientific research would facilitate its implementation.[3]

The witnesses at the hearing were as follows:

Congressman Don Fuqua, Chairman, Committee on Science and Technology.

Ronald E. Cape, Chairman and Chief Executive Officer, Cetus Corporation.

Martin Alexander, Professor, Department of Agronomy, Cornell University.

Robert M. Goodman, Vice President of Research and Development, Calgene, Inc.

Robert K. Colwell, Professor, Department of Zoology, University of California.

Brian P. Crowley, Senior Associate Director, Resources, Community, and Economic Development Division, U.S. General Accounting Office.

David T. Kingsbury, Assistant Director, Biological, Behavioral, and Social Sciences, National Science Foundation.

John A. Moore, Assistant Administrator for Pesticides and Toxic Substances, U.S. Environmental Protection Agency.

John Patrick Jordan, Administrator, Cooperative State Research Service, U.S. Department of Agriculture.

A. Background

In December 1984, the Administration published guidelines for the regulation of releases of genetically-engineered products outside of laboratory confinement.[4] The proposed policy relied on existing statutory authority to address the particular concerns raised by biotechnology. This reliance on existing authority raised questions regarding agency jurisdiction and regulatory authority. In addition, by December of 1985, uncertainty regarding various agencies' review of the initial applications to release genetically-engineered organisms into the environment lead to concern regarding the implementation of the Proposed Coordinated Framework.

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[3] "Hearing: Planned Releases", *supra,* note 11, Part I.

[4] 49 Fed. Reg. 50856.

B. Discussion

1. Industry's experience with the proposed coordinated framework

At the hearing, industry representatives discussed their experience in seeking federal approval for field tests of genetically-engineered organisms. Dr. Ronald Cape, founder and Chief Executive Officer of Cetus Corporation, recounted the problems that Agracetus Corp. (a subsidiary) encountered in voluntarily seeking federal authorization to test a genetically-modified plant under field conditions. In 1984, the Plant Working Group of the NIH Recombinant DNA Advisory Committee (RAC) had reviewed the Agracetus proposal, but a pending law suit prevented RAC from authorizing the field test.[5] In an effort to obtain official approval of their plan, the company submitted the proposal to the Animal and Plant Health Inspection Service (APHIS), a regulatory division of USDA. Dr. Cape then discussed the difficulties Agracetus encountered in seeking authorization from USDA for its proposed field test:

Dr. Cape. Agracetus provided additional information to APHIS during this time to further document the RAC review and the protocol to be followed. On June 14, 1985, APHIS wrote to Agracetus indicating that APHIS staff had completed its review of our proposed experiment and found that, based on our protocol, our test did not constitute a plant pest risk and would not be subject to further regulation by USDA, APHIS under the Plant Pest Act.

Upon review by our attorneys of the USDA letter, we determined that we did not yet have an actual approval to conduct our test. Although the APHIS determination was favorable, in that it found our test would not constitute a plant pest risk, *the agency did not yet have a mechanism to grant us the authority to go ahead.* In our view this was because APHIS had not yet publically set forth the policies and procedures that would knit together their various authorities detailed in the December 31, 1984, Federal Register notice. Although it was clear that such policies existed at least in prototype form within the Department, we believed that given the novelty of our experiment and given the extent to which the whole regulatory question about biotechnology was being debated, it would be perferable for us to proceed with a test only in circumstances of a generally known and accepted review mechanism. Thus, as of early July we made the decision to defer beginning experimental tobacco until either the APHIS process was published and opportunity for public review had been provided, or until our original application before the NIH was approved by the NIH director in accordance with the RAC Guidelines.[6] [Emphasis added.]

In July 1985, it became clear that USDA would not take any regulatory action on the company's application. Subsequently Agracetus submitted its proposal to the NIH/RAC.

Dr. Cape. . . . as you know, it's a rather strange situation in that industry is not, strictly speaking, required to adhere to every last sentence including the sign-off from the Director. But there was no way in which we were going to try to short cut the last dot on the last "i" which meant that even though we got the scientific green light from RAC, until Dr. Wyngaarden was willing to give us the same approval that he would give to an NIH-funded lab, we weren't about to move.[7]

Dr. Kingsbury, chairman of the BSCC, underscored the reliance on voluntary compliance by industry with the NIH Guidelines:

Dr. Kingsbury. There's no requirement that they tell us anything. The courtesy and the position of the industry in the past has been to voluntarily follow the NIH guidelines and to voluntarily bring those to the NIH prior to the application. As Dr.

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[5] *Foundation on Economic Trends* v. *Heckler,* 587 F. Supp. 753 (D.C. 1984) 756 F. 2d 143 (D.C. Cir. 1985); *See also,* Appendix A, *infra.*

[6] "Hearing: Planned Releases", *supra,* note 11, Part I, at 215.

[7] *Id.,* at 93.

Cape was describing, . . . they were unwilling to go into the environmental applications, even for stage I (One) testing, without going to the NIH for approval.[8]

In December 1985, Dr. James Wyngaarden, Director of the NIH, officially approved the Agracetus field test proposal.

Another industry witness, Dr. Robert Goodman, Vice President of Research and Development of Calgene testified that he anticipated fewer problems in gaining USDA approval for the field test of a genetically-altered plant developed by his company.

Dr. GOODMAN. Well, we made our application some months ago when the situation was less clear than I think it is today, and well after the application that Dr. Cape is referring to, and we didn't know for sure where to go, and so we sent our application to Secretary Block.

Mr. VOLKMER. And what was the result of that?

Dr. GOODMAN. As I understand the result of that, the application was husbanded to the Assistant Secretary for Science and Education. The committee within USDA, which was referred to as the Agricultural Recombinant DNA Advisory Committee, was at least briefly—sometime toward the end of the summer—assigned the responsibility for it. That group, as it is presently constituted and as I understand it, includes people from APHIS as well as from other USDA and outside of USDA agencies. The situation has developed over the last several months. I believe that in the end, APHIS is likely to have—is likely to contribute what we hope will be approval, which we expect perhaps in the *next week or two.*[9] [Emphasis added.]

The fact that Agracetus delayed its field test plans for three years while waiting for government authorization for the experiment was of great concern to the Subcommittee.

Mr. PACKARD. And apparently, then, there is the feeling in the industry that there are impediments and there are stumbling blocks that our industries are required to move through that are facilitated in foreign countries?

Dr. CAPE. Yes. . . . What we're looking for is a well-recognized sequence of events that corresponds to what goes on in the testing of a new drug, and each stage—until the very last—is an experiment, and each stage sets the stage for the next stage, depending on the results. We felt that we're stymied at a very early stage. We're not permitted to perform the experiments.[10]

This concern was also apparent in Dr. Goodman's comment:

Dr. GOODMAN. What we're facing, with respect particularly to plants and other agricultural applications, is the fact that the path is not that clearly elucidated, and also the fact that it is not a contained operation. When we go to agriculture, we go to the field by definition and by necessity, and I think there has been, . . . a lot of muddled thinking and some significant delays that, if they continue, represent a serious concern.[11]

Both Drs. Cape and Goodman supported the development of a rational regulatory system in general[12] and the Proposed Coordinated Framework in particular.[13] However, both expressed concern that excess and premature restrictions on field tests would retard the United States' biotechnology industry and thereby benefit competing nations.[14] They urged that the government be "a facilitator of bringing safe products to the market, domestically and internationally, and not a roadblock."[15]

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[8] *Id.*, at 179.

[9] *Id.*, at 95 and 216. Six weeks following the hearing, the Subcommittee learned that USDA would shortly approve the field test. "We have been informed that our application has been reviewed and approved by the USDA, and should receive the formal notification of approval by January." *See also* Appendix A, *infra.*

[10] *Id.*, at 85.

[11] "*Id.*, at 87.

[12] *See*, "Hearing: Planned Releases", *supra,* note 11 Part I at 27 and 56, respectively.

[13] *Id.*, at 29 and 54.

[14] *Id.*, at 23.

[15] *Id.*, at 32.

2. USDA REGULATION OF BIOTECHNOLOGY

The testimony of Drs. Cape and Goodman indicated that there were some problems with USDA's regulation of biotechnology. These regulatory problems at USDA were discussed more fully in testimony provided by Mr. Brian Crowley, Senior Associate Director, Resources, Community, and Economic Development Divison of the General Accounting Office (GAO).

Mr. Crowley described the findings of a GAO investigation conducted at the request of the Committee on Science and Technology.[16] This report analyzed the role of USDA as both regulator and promotor of biotechnology research. It was found that during FY 1984–1985, USDA funded $40.5 million in biotechnology research. Eighty-seven of the 778 projects funded, had as their intent, the release of genetically-engineered organisms into the environment within the following 5 years. Only 3 of these research projects addressed risk assessment as an integral part of the research plan.

Several USDA witnesses addressed the issue of USDA's preparedness to regulate biotechnology products. Dr. John Wood, Assistant Administrator of the Animal Plant Health Inspection Service (APHIS), who accompanied Dr. Patrick Jordan, Administrator of the Cooperative State Research Service within USDA, sought to resolve for the Members the apparent confusion concerning the Department's review of biotechnology products:

Dr. WOOD. . . . At the present time, the APHIS . . . has its regulation relative to the movement of genetically engineered plants from the laboratory to the field. We consider that in an interstate situation to be a movement by definition.

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We are working with the State department of agriculture, in particular the California Department of Food and Agriculture, relative to this.

Mr. VOLKMER. OK. Then, in other words, the two of you are basically satisfied that plants will not be introduced that have been genetically altered without some kind of a notice to USDA. Is that correct or incorrect?

Dr. WOOD. I believe that's correct from this standpoint. If, in fact we know of it or they have applied for a permit, yes, we would know about it.

Mr. VOLKMER. Well, if you have no notice of it and they don't notify you of it, in any extent, how would you know about it?

Dr. WOOD. You wouldn't.

Mr. VOLKMER. What would you do if they did it?

Dr. WOOD. We do have a monitoring and compliance requirements, you know. We are working directly with the States in this particular manner. In addition to that, we do have a survey group, within the plant protection quarantine which works directly with the Land Grant Universities as well as the State departments of agriculture for surveys for pest presence on a continuing basis.[17]

Dr. Wood told the Members that in order to approve a field test, the department would have to make sure that the organism would not be harmful to agriculture.

Mr. VOLKMER. How would you find out if it's harmful or not?

Dr. WOOD. Through the use of hazard analysis.

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Mr. VOLKMER. How long would that take?

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[16] *See,* "USDA's Biotechnology Research", *supra,* note 1, Part I.

[17] "Hearing: Planned Releases", *supra,* note 11, Part I, at 177.

Dr. WOOD. Well, based on what we've seen to date, I believe we have done a good job on evaluating the hazards of the products that have come in, and we can do it in about 10 days.[18]

Dr. Jordan added that any uncertainties perceived in the USDA policy statement in the Proposed Coordinated Framework had been resolved by a directive from the Secretary of Agriculture:

The Secretary of Agriculture last July, Congressman, put forth a delegation of authority which renders all of those things related to regulation under the Assistant Secretary for Marketing and Inspection Services, and all of those things which are relevant to research only under the Assistant Secretary for Science and Education.[19]

3. EPA REGULATION OF BIOTECHNOLOGY

In contrast to the situation which existed at USDA at the time of the December 1985 hearing, EPA had already reviewed several applications and given one approval for a field test. These reviews were conducted by Science Advisory Panels that evaluated the risks posed by specific releases. The importance of risk assessment research in evaluating these proposed releases was discussed by Dr. Martin Alexander, Professor, Department of Agronomy, Cornell University and Chairman of EPA's Study Group on Biotechnology. Dr. Alexander described the major components of risk assessment research in biotechnology as follows:

Four risk components are relevant to genetically engineered species that are deliberately released for agricultural uses or into natural environments. These are: (1) the possibility that the organism will survive following its release, (2) the likelihood that it will mulitply in some natural environment or in farmed areas, (3) the possibility that it will be dispersed and make contact with species that it can injure, and (4) the chance that it will be harmful.[20]

Information on these points provides a researcher with guidance in designing conditions under which an organism can be safely used in the environment. After questioning by Congressman Brown, Dr. Alexander went on to explain why risk assessment should be an integral portion of research involving organisms proposed for release into the environment:

Dr. ALEXANDER. *We are operating with an enormous lack of knowledge on the behavior of introduced species,* and if we had that knowledge—and I don't think we should stop introducing new organisms because of the absence of knowledge—but if we had that knowledge, I think we would reduce the potential for a problem and accentuate the benefits for those organisms—plants, animals, or micro-organisms—which will be beneficial to society.

So whether it requires a specific congressional mandate or action by individual agencies, I think we do need to have information on which to base our conclusions, and some tests which determine whether the information—the generalizations—are appropriate for particular products.

Mr. BROWN. Well, does this mean that we need to build into each of the approved field tests a larger component of ecological research? Or are the research protocols being built in now—and I'm totally ignorant of this—adequate to give us this information that you say we need?

Dr. ALEXANDER. There are no research protocols now. I don't think that field testing should involve meaningful research, because then it's already too late. *The research should be done, at this time, parallel to the introduction of new products, and the data should be available, such that when we do have a larger number of prod-*

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[18] *Id.*, at 180.
[19] *Id.*, at 181.
[20] *Id.*, at 40.

ucts, we will have a basis for deciding whether appropriate tests should be run, or whether materials should be deliberately released.[21] [Emphasis added.]

In one specific case, Advanced Genetic Sciences, Inc. (AGS), of Oakland, CA, notified EPA it planned to test whether a microbe called "ice-minus" would inhibit frost formation on strawberry plants under field conditions. The agency required that AGS apply for an Experimental Use Permit (EUP). Approval for the field test was granted in November 1985, but the field test has yet to occur.[22]

Dr. John Moore, Assistant Administrator for Pesticides and Toxic Substances of the EPA, described the process the Agency used in evaluating the AGS application:

More importantly, in approving the AGS experiment, we did engage in an extensive peer review process, utilizing experts from both inside and outside the Federal Government, and provided them an opportunity for public comment. I would suggest that *this review and evaluation procedure served to identify and address the potential risks associated with this specific proposal, and that indeed this type of review process will, at least for the foreseeable future, become the norm within EPA for reviewing biotechnology proposals, and not the exception.*[23] [Emphasis added.]

EPA convened an *ad hoc* panel of experts to augment its existing Scientific Advisory Panel to thoroughly review the AGS application. Two members of that panel, Dr. Robert Colwell, Professor of Zoology, University of California, and Dr. Martin Alexander, testified before the Subcommittee concerning their participation in the EPA review. Dr. Alexander testified that EPA seemed to be moving forward in an effort to thoughtfully regulate the use of genetically-altered microorganisms in the environment:

Let me also add that the regulatory staff of EPA, I believe, has done a commendable job in setting up a regulatory framework, but this they have done with a very skimpy data base and with no generally-accepted procedures for testing biotechnology products. It is to be hoped that their activities will be bolstered, and their approach will be modified, as new information develops and as tests are initiated and are conducted in a generally-acceptable fashion.[24]

Dr. Colwell described the sharp contrast he observed between the review processes at EPA and USDA:

From my own experience in reviewing proposed environmental testing of genetically engineered organisms for both the EPA and the USDA (the latter very recently), I am left with two distinctly different 'flavors', even though both agencies were very thorough in the evaluations in which I have so far participated. The EPA process, while explicitly recognizing the importance of balancing risk against potential scientific economic gains (rather than forbidding any release that could even conceivably cause the slightest environmental mischief), maintained an air of impartial judgement—I felt that each case could go either way. In contrast, the USDA officially (FR Dec. 31, 1984, p. 50898) takes the position that 'these products (of genetic engineering) are not fundamentally different from products obtained by co(n)ventional technology' and rather clearly finds the special NIH guidelines for plants modified through recombinant DNA techniques as quite unnecessarily onerous, although the U.S.D.A. is committed to following them, for the time being. (New crop varieties produced by conventional breeding are subjected to no such ecological inquisition).[25]

At the time of the hearing the underlying philosophy of USDA and EPA with regard to assessing the products of biotechnology was fundamentally different. For example, in discussing EPA's ap-

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[21] *Id.*, at 90.
[22] *See* discussion *infra*, Part II, Chapter Two and Appendix A, *infra*.
[23] "Hearing: Planned Releases", *supra*, note 11, Part I, at 152–53.
[24] *Id.*, at 36.
[25] *Id.*, at 81.

proval of the the ice-minus bacteria, Dr. Moore described the calculations the Agency makes in evaluating an application as follows:

EPA believes that the development of risk assessment guidelines will be aided by the experience gained in conducting case-by-case evaluations and by the data gained from conducting carefully planned and controlled field tests with those genetically altered micro-organisms determined to pose minimal risks. The Agency's ultimate aim is to design a formal method for predicting effects and for evaluating potential risks.[26]

Contrast this with the declaration by Dr. Jordan of USDA:

In USDA, we have identified three conceptual precepts which provide policy direction for our further actions. We believe first, that *agricultural and forestry products developed through modern biotechnology will not differ fundamentally from products devleoped through conventional procedures;* second, that the Department has adequate statutory authority to provide research oversight and product regulation; and third, that we must make all prudent efforts to ensure that new plants, animals, and microorganisms are introduced safely into the environment.[27] [Emphasis added.]

Dr. Jordan's remarks are in accord with the Department's policy as stated in the Proposed Coordinated Framework. *"To date, no unique or safety problems have been associated with products of genetic engineering, conventional or modern."*[28] [Emphasis added.]

Congressman Brown, citing certain problems associated with conventional crop development programs, questioned the agencies' willingness to recognize potential problems associated with new technological developments.

Mr. BROWN. Let me just say something that shouldn't need to be said: none of the members of this committee are anti-science or anti-technology. We are strong supporters of it. But also, most of us have been around long enough to have preceived occasional situations where something went wrong. I don't see in any of your testimony any reflection of the possibility that something could go wrong.

For example, in the long history of 100 years of agricultural research, have you never done anything wrong?

. . . You take the earlier generation of genetic manipulation which resulted in the development of things like hybrid corn. That was a great boon to the corn growers, and yet it produced a blight which had a destructive effect on the corn industry until we found a solution to the blight.

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Mr. KINGSBURY. *There certainly is a point that uncontrolled widespread release of a newly engineered organism that had a dire effect could no longer be recalled.* . . . A plant is not likely to have the inapparent and uncontrolled spread that a recombinant influenza virus might have in an animal population where we don't know it's going on. It's a much different situation. Certainly, an engineered microbe introduced into the environment has to be very carefully controlled.

Mr. BROWN. Well, I think you're right, that the problem of plant genetic variations is not as serious as microbiological—but you're working in both of these. The science is contemplating the possibility of developing a strain of nitrogen-fixing baceteria which might be inserted into plants. Now, wouldn't this have a massive effect on the ecological niche that those plants could occupy if they are given the capability of extracting their own nitrogen from whatever——

Dr. KINGSBURY. Indeed. There, we're looking at a construction that could have a real effect on plant(s) . . . rate of growth and its site of growth (which) could be quite dramatically altered.[29] [Emphasis added.]

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[26] *Id.*, at 152–53.
[27] *Id.*, at 166.
[28] Fed. Reg. 50856 at 50897.
[29] "Hearing: Planned Releases", *supra,* note 11, Part 1 at 169 and 170.

Dr. Colwell summed up the problems by suggesting that USDA's efficacy is compromised by its mandate to both promote and regulate biotecholnogy:

> Dr. COLWELL. This brings me immediately to what I see as the single most problematic aspect of the USDA's role in agricultural biotechnology: It tends to play both quarterback and umpire at the same time. Traditionally, the USDA has seen itself as not only an active promoter (and funder) of basic research, but also as a sort of traveling salesman of applied technology, working closely with seed companies, agrochemical firms, and farm machinery manufacturers to achieve the laudable goal of helping America's farmers and ranchers to maximize their productivity. I anticipate that in 5 years, Agricultural Extension agents will be promoting the use of genetically-engineered crops, farm animals, and microbial inputs. Meanwhile, we are assured by unnamed "knowledgeable ARS (Agricultural Research Service) official(s)" and unnamed Assistant Administrators that approval to release genetically-engineered organisms would not be given without careful scrutiny.[30]

C. SUMMARY

The testimony at the hearing presented a picture of regulatory certainty and thoroughness. Industry witnesses judged the Proposed Coordinated Framework to be a good first step toward a rational regulatory system that would facilitate the development of safe biotechnology products. Even more encouraging was the assertion by the agencies and the OSTP, that new regulatory guidelines would be published in the Federal Register by January 31, 1986. Unfortunately, events of the next several months depicted the problems researchers and federal agencies encountered in following and implementing biotechnology regulations.

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[30] *Id.*, at 80.

CHAPTER TWO: "ICE-MINUS": A CASE STUDY OF EPA'S REVIEW OF GENETICALLY-ENGINEERED MICROBIAL PESTICIDES

On March 4, 1986, the Investigations and Oversight Subcommittee held a hearing to investigate an apparently unauthorized environmental release of a genetically-engineered microbial pesticide.[31]

Witnesses at the hearing were as follows:

Dr. John R. Bedbrook, Vice President and Director of Research, Advanced Genetic Sciences, Inc.

Mr. Steven Schatzow, Director, Office of Pesticide Programs, U.S. Environmental Protection Agency.

Dr. Robert Colwell, Professor, Department of Zoology University of California.

Hon. Leon Penetta, U.S. Congressman from the State of California.

Mr. Sam Karas, Chairman, Monterey County Board of Supervisors, accompanied by Mr. Walter Wong, Director of Environmental Health, Monterey County, California

Mr. Glenn Church, President, Action League for Ecologically Responsible Technology (ALERT).

A. Background

Scientists at Advanced Genetic Sciences, Inc. (AGS), in collaboration with scientists at the University of California, Berkeley, isolated and removed the gene responsible for ice formation from two naturally occurring strains of the bacteria *Pseudomonas.* When this gene-deleted bacteria, referred to as "ice-minus", is sprayed on plants, ice crystallization forms at a lower temperature than normal, thereby reducing frost damage to crops.

In November 1984, AGS applied to EPA for an Experimental Use Permit (EUP) under FIFRA to do a small scale field test of ice-minus on a 0.2 acre plot of strawberries in Northern California.[32] EPA convened a meeting of a subpanel of the Scientific Advisory Panel (SAP) to review AGS' application. In February 1985, EPA asked AGS to provide additional data on plant pathogenicity, the proposed test plot and the proposed test conditions.[33] AGS submit-

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[31] "Hearing: Ice-Minus", *supra,* note 12, Part I.

[32] *See* Memorandum of Stanley H. Abramson to Don R. Clay on the Applicability of FIFRA or TSCA to Microbiological Agents Used to Control Ice Nucleation, found as Appendix C to "The Environmental Implications of Genetic Engineering", *supra,* note 15, Part I; *See also,* Appendix A, *infra.*

[33] Notification to EPA to do a small field test typically includes detailed information on the test and the microbe to be tested, including identity, natural habitat, host range, growth and survival, effects on non-target organisms, and for genetically-engineered microbes, information on construction, potential for genetic transfer, and competitiveness. Additionally, information on the location of the test site, its size, what occurs there naturally, and descriptions of monitoring, containment and disposal methods are required. Upon notification, the Agency will have 90 days to evaluate the notice. Applicants would be free to perform their field test after that time period unless otherwise informed by the Agency.

ted this data in July 1985. After review by many groups both inside and outside EPA, including USDA, FDA, and NIH, EPA granted the EUP on November 14, 1985. AGS prepared to conduct its field test in North Salinas Valley in Monterey, California, in early 1986.

However, in February 1986, the Investigations and Oversight Subcommittee learned that AGS, prior to receiving the EUP, had conducted unauthorized outdoor experiments with the genetically-engineered "ice-minus" microbe. According to information obtained by the Subcommittee, AGS, in early 1985, performed the pathogenicity tests requested by EPA by injecting the genetically-engineered microbes into trees located on the rooftop of their office building.[34] Data from the rooftop experiment was used to support AGS' application for the EUP to conduct the small-scale field test. At the hearing, the Subcommittee investigated whether there had in fact been an unauthorized environmental release of the microbe, whether data from the experiment should be relied upon to support the grant of the permit, and whether EPA and AGS had shown sufficient caution in choosing the test site.

B. Discussion

1. THE ROOFTOP EXPERIMENTS

Dr. John Bedbrook of AGS testified at the hearing that all the tests EPA required, with one exception, were conducted inside AGS' greenhouse facilities.[35] The exception was a test conducted on the roof outside the greenhouse to determine whether the altered bacteria was pathogenic to several types of fruit trees.

Dr. Bedbrook testified that the location of the one outdoor experiment was chosen in consideration of the duration and physical space requirements. In addition, he testified that those involved felt their experimental design adhered to the interim policy requirements, and that they made a conscious decision to proceed.[36]

> Dr. Bedbrook. The management group controlling this particular set of experiments included the officer or manager of regulatory affairs, and he distributed to all of the people involved in that management team the interim guidelines at some time soon after they were made available. Adherence to those guidelines was implicit in that management group. However, the two researchers which I have referred to earlier discussed and deliberated on the issue of whether or not they should conduct this experiment in the manner that they did, and they came to the conclusion that they should proceed.
>
> So, they did that knowledgeable of the guidelines, having read the guidelines, and decided to proceed with the tests.[37]

When asked why AGS failed to notify EPA about the rooftop tests, Dr. Bedbrook replied that AGS' scientists did not consider the outdoor experiment to involve a "release" of the altered bacteria.[38] Dr. Bedbrook testified that the company felt the woody tissue of

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[34] *See* "Hearing: Ice-minus", *supra,* note 12, Part I, at 5 and Appendix 4 at 137. In early March, the Subcommittee received a letter from an ex-employee of AGS who had been directly involved in the roof-top experiment. Information in the letter detailed what the author considered to be problems with the experimental design and overall scientific practices at the company.

[35] *Id.,* at 5.

[36] *Id.,* at 20. *See* discussion of interim policy, *supra,* Part I.

[37] "Hearing: Ice-minus", *supra,* note 12, Part I, at 46.

[38] *Id.,* at 37.

the tree adequately contained the microorganism, which does not replicate and proliferate within a tree.[39]

The NIH Guidelines applicable to AGS' laboratory research require no specific physical containment for this type of microorganism. The guidelines generally require "good microbiological practice".[40] However, EPA's interim policy for research involving genetically-engineered microbial pesticides requires tests of this sort to be conducted in a laboratory or a containment facility.[41]

Mr. Steven Schatzow, Director of EPA's Office of Pesticide Programs, testified that EPA felt the rooftop experiments violated EPA's interim policy. ". . . we all have an idea of what a contained facility is, I think, and laymen, I think, would agree that a tree does not meet that definition".[42] Congressman Packard questioned whether the interim guidelines and regulations were clear enough to enable AGS to comply with them:

Mr. PACKARD. Do you feel that your interim guidelines and regulations are clear and adequately outline the problems and the requirements of any company such as AGS?

Mr. SCHATZOW. On this issue I think it is very clear, yes.

Mr. PACKARD. As an aftermath of this whole incident and this hearing, do you sense or see that there will be a need to revise or to change your guidelines?

Mr. SCHATZOW. I don't see the need to revise or change the guidelines. I see a need perhaps for better public dissemination of the guidelines and better education of some of the scientists that are working in this area.

Mr. PACKARD. That was my next question. Do you believe that AGS was totally and adequately informed as to the requirements?

Mr. SCHATZOW. Well. I think AGS was clearly informed. They testified that they were. They submitted to us a notification and response to the interim policy. They were obviously aware of it at the corporate level, and, according to the testimony earlier today, their individual scientists were aware of it.

Mr. PACKARD. They were aware of it. Now they did also testify that they actually discussed it at the decision making level as to whether they should notify EPA and they made a deliberate decision that it wasn't necessary.

Mr. SCHATZOW. That is what I thought I heard, too, Congressman, yes.

Mr. PACKARD. That brings up, then that same question. Are the reg(ulation)s clear enough that it would avoid a repeat of this kind of an incident?

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Mr. SCHATZOW. Well, that seems to be maybe part of the problem. I am not sure. If you or I were asked when you read something in sequence that talks about laboratory, contained laboratory, growth chamber, greenhouse, or other contained facility, if you were taking your Miller analogy test and someone then said tree, . . . does that go in the same group, you or I would probably say I don't think so.[43]

In response, Dr. Bedbrook testified that:

The controversy surrounding the outdoor test did not arise as a consequence of any inadequacy of the EPA interim policy nor as a consequence of any conscious disregard of that policy by AGS scientists.[44]

Testimony did demonstrate that there presently is no clear, working definition for "containment". Mr. Schatzow testified that the notion of complete containment was an elusive concept, and that no one could guarantee that unauthorized releases would not occur in "contained" experiments. The issue, according to Mr.

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[39] *Id.*, at 38.
[40] "NIH Guidelines", *supra*, note 6, Part I.
[41] 49 Fed. Reg. at 40659–40661.
[42] "Hearing: Ice-minus", *supra*, note 12, Part I at 84.
[43] *Id.*, at 84–85.
[44] *Id.*, at 6.

Schatzow, is one of various *levels* of containment.[45] From his testimony, Mr. Schatzow indicated the EPA did not consider a tree to be an acceptable level of containment.[46]

2. VALIDITY AND RELIABILITY OF AGS EXPERIMENTAL DATA

AGS tested the possible pathogenicity of the altered bacteria by injecting four kinds of material into small branches of several types of fruit trees. The trees were injected with 1) a naturally occurring "ice-plus" (ice-forming) bacteria; 2) the experimental "ice-minus" bacteria; 3) a bacteria known to cause pathogenicity (to serve as a positive control); and 4) saline solution to serve as a negative control. AGS observed the trees for up to 7 months.[47]

Dr. Robert Colwell, who served on EPA's Scientific Advisory Panel to review the AGS application, questioned why AGS needed to conduct the tests at all considering its attitude about the safety of the organisms.

Dr. COLWELL. . . . did any harm come of doing them on the rooftop? Well, if it is true that they weren't pathogenic, then I feel no hesitation in saying that no harm came from it. However, assuming that they aren't pathogenic and then saying it is OK to do it on the rooftop because we know they aren't pathogenic when you are testing pathogenicity just doesn't fly in terms of logic.

In fact, in the statement of AGS today, in their written statement, we find this sentence about the workers in this project. "They were confident that the test organisms were not pathogens and therefore would not multiply in the fruit tree tissues". *One might well ask why they are doing the test if they are already confident that they are not pathogens.*[48] [Emphasis added.]

Testimony at the hearing indicated several breaches of accepted scientific practice on the part of AGS officials. The rooftop tests were done under completely uncontrolled humidity and temperature conditions. This not only violated standards of good scientific practice, but also violated the conditions EPA required for the experiments.

Dr. COLWELL. In their application for an EUP, I want to read you two statements. This is for the pathogenicity testing: "Plants were incubated in a greenhouse at approximately 21 plus or minus 5 degrees centigrade on elevated benches without misting or under moist conditions as recommended." No qualification for some of them being out of the greenhouse on the rooftop in different temperatures.

. . . Table 1f is entitled, "Inoculation Methods for Tests of Pathogenicity to Plants." The first line in the table is branch injection of cherry, peach, apricot, plum, almond, and pear. There is a footnote to the entire column of inoculation including this that says "Plants were incubated on greenhouse bench and/or under moist conditions at 21 plus or minus 5 degrees centigrade as recommended by referenced publication."

Now, the only possible escape from, I would say, intentionally misleading the panel is the "or" under the slash in the "and/or". However, it does state clearly that it was 21 plus or minus 5 degrees centigrade. I live in Berkeley. In February of any year, it goes much colder, and this year, it went up to 80 degrees. *There is no way that that indicates to anyone reading this that those are anything but greenhouse conditions.*[49] [Emphasis added.]

Dr. Colwell explained the purpose of reviewing environmental releases of genetically-engineered organisms, and how he felt AGS had undermined that process.

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[45] *Id.*, at 86.
[46] *Id.*, at 84.
[47] *Id.*, at 19.
[48] *Id.*, at 90.
[49] *Id.*, at 89 citing Table 1f, Appendix 2 at 135.

Dr. COLWELL. *The purpose of the EPA review prior to testing genetically-engineered organisms in the open environment is to permit disinterested scientists from a carefully chosen set of disciplines to evaluate each case for the safety of the proposed test and for the benefit and protection of society at large.* It is impossible to carry out this task without full and detailed disclosure of all relevant information by the applicant. If the judgment of safety, and what results are important, is made ahead of time by the applicant, this process is derailed.

From my own point of view, I am very concerned and troubled by finding out that what we believed to be true in reviewing the case on the basis of submissions to EPA has turned out not to be accurate . . .

I won't speculate on the motivations of the company for not reporting that they did this on the rooftop. All I can say is that every member of our committee and everyone at the EPA who read the report assumed that these tests were done in the greenhouse.[50] [Emphasis added]

In addition to the uncontrolled experimental conditions, there was a problem in the way AGS administered the positive controls.[51] AGS inoculated certain trees with both the genetically-altered bacteria and the positive controls, simultaneously. Additionally, some species of trees that received the altered bacteria were never injected with the positive control due to the unavailability of *Pseudomonas syringae* pathogens of the proper type.[52]

Some inoculations were made after the optimal time for pathogenicity tests, i.e., when the trees were no longer dormant. In non-dormant trees, canker development is restricted, so that even some trees injected with the positive control in the non-dormant state failed to show positive results, i.e., cankers. The ineffectiveness of the positive control undermines any conclusions drawn from the absence of a pathogenic response to the experimental bacteria.[53]

As evidence of further questionable practice, AGS scientists used for their experiments "clean" branches from trees whose other branches showed symptoms of possible disease. It was further revealed that some of the trees used in the rooftop experiment had been used in earlier studies.[54] The trees were not individually tagged at that time, so it could not be determined which ones had been re-used in the rooftop experiment. Some plant pathologists believe that completely healthy trees should be used to be certain of reliable test results.[55]

It was also noted that a limb on which an adverse reaction was seen was supposedly pruned by accident and disposed of. No attempt was made to examine the site of the adverse reaction. Additionally, both the EPA and an ex-employee noted that the quantity of bacteria injected into the tress was decreased midway through the experiment.[56]

The rooftop experiments also included a certain species of cherry tree. Data from these injections were not included in the EUP ap-

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[50] *Id.*, at 89.

[51] Positive controls are organisms known to be pathogenic to the host in question. They are used to confirm that the conditions under which the tests are performed are conducive to the development of a pathogenic reaction. If no reaction occurs in response to an organism known to cause one, then the test conditions are questioned.

[52] *See* "Hearing: Ice-minus", *supra,* note 12, Part I, at 40.

[53] *Id.*, at Appendix 5 at 139; Correspondence between Investigations and Oversight Subcommittee and EPA.

[54] *Id.*

[55] *Id.*

[56] *Id.*, Apparently the supervisor was unaware of this and there was no indication in the technicians notebook of how these dilutions were made. It is possible that this could have been a cause of the lack of reaction in certain positive controls.

plication for unknown reasons. Evidence from EPA's investigation revealed no consistency at the company regarding maintenance of laboratory notebooks.[57]

Due to these lapses in good experimental practices and the unreported, uncontrolled weather conditions, the question arose whether any cankers had resulted from the rooftop test and subsequently went unreported to EPA. At the hearing, Dr. Bedbrook said that, ". . . if any spurious response was obtained from injection with these organisms, they were ultimately extracted. There was an attempt to recover those organisms from that tissue, and we failed to ever see any. This is how we defined, or part of how we defined, that these were not pathogenic to these species." [58] In addition, information supplied to EPA in the EUP, from tests done on a series of fruit trees revealed that "no pathogenic reaction, infectivity, or phytotoxicity was evident in these tests on either the parental or ice-minus derivatives." [59] Dr. Bedbrook also pointed out at the hearing that any true cankers only occurred as a result of the positive control.[60]

Information supplied to the Subcommittee contradicted this.[61] An ex-employee involved with the specific tests asserted that there had been a small canker near the injected areas on both a Cherry and Texas Mission Almond trees. He suggested that bacteria be isolated from the wounds, but it was never done. He attempted to do it once himself but was unsuccessful. In fact, he asserts he was ordered to decrease the inoculum size for future inoculations.

3. TEST SITE LOCATION

Both the EPA staff and the Scientific Advisory Panel determined that AGS should conduct its experiment at a remote site.[62] When informed of this request, AGS assured the Scientific Advisory Panel that it would conduct the test in "remote locations".[63] However, because the truly remote sites were either unsuited to strawberry propagation due to soil conditions or other environmental factors, or were so far removed from their headquarters to make the logistics of the experiment extremely difficult, AGS told EPA it would pick a site "temporally" remote from the blossoms of plants that would support the growth of "ice-minus."[64] Thus, at the time of the intended test, fruit trees in the area would not be in bloom.

EPA did not visit the test site prior to approval of the EUP in November 1985. However, after the EUP was granted, EPA personnel did visit the site in order to specify the location of the equipment necessary to monitor the course of the field trial as specified in the EUP.[65] The Agency discovered that the test site was in a

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[57] *Id.*
[58] *Id.*, at 42.
[59] *Id.*, at 43, and Table 1g, Appendix 2 at 136.
[60] *Id.*, at 43.
[61] *Id.*, at Appendix 4 at 137.
[62] *Id.*, at 80. EPA cannot require a specific site selection, but can set conditions to protect health, safety, and the environment.
[63] Advanced Genetic Sciences, Inc., submission in support of its Experimental Use Permit application, July 2, 1985, at Section G.
[64] *Id.*
[65] *See* "Hearing: Ice-Minus", *supra*, note 12, Part I, at 56.

residential area, within one-half mile of 10,000 people and close to major agricultural areas.[66] EPA did not ask AGS to relocate the test site at that time. Instead, because the test site was in a residential area, EPA asked AGS to obtain easements from the adjacent property owners in order to set up its monitoring equipment. EPA also required AGS to advise the adjacent land owners in writing of the proposed experiment at least 15 days prior to its initiation.[67]

Dr. Colwell testified about his reaction to the fact that the "remote" test site was in a residential area: "We simply didn't look and demand to look at the test site because of the assurance of the company that it would be a remote site. . . . I assumed that by remote they meant something much different from what it turned out to be." [68] Presently there exists no standard definition of an "isolated and remote area." [69]

Congressman Leon Panetta, and Dr. Colwell presented evidence at the hearing that there were other areas of the county more isolated and more appropriate for such an experiment.[70] Mr. Panetta also expressed concern with EPA's failure to visit the test site: ". . . given the uncertainties involved with this new technology, and this was the first test to take place in an open field, EPA I think, should have proceeded with greater caution and should have had a site evaluation of the test itself". [71] One possible reason for selection of the particular site was provided at the hearing. Dr. Bedbrook stated that the owner of the test site was, "indeed one of us", implying it was someone affiliated with the company.[72]

4. COUNTY GOVERNMENT

Although both EPA and the California Department of Food and Agriculture had approved AGS' proposed field test, the Monterey County Government and populace only learned about the experiment through media accounts in December 1985—after EPA had granted the EUP. At a public hearing, local residents expressed fear and suspicion about the test, especially because AGS refused to reveal the precise location of the test site, because it was "confidential business information". County citizens and county government officials were especially chagrined to learn that federal and state representatives had not visited the test site before approving the experiment. Because Salinas Valley is one of the most productive vegetable growing areas in the country, the Monterey County Board, uncertain of the experiment's safety, placed a moratorium on the experiment under its authority to regulate both environmental waste and air pollutants.[73]

The actions by EPA and the State of California aroused a great deal of mistrust on the part of local elected officials and the

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[66] *Id.*, at 105.
[67] *Id.*, at 56.
[68] *Id.*, at 89.
[69] *Id.*, at 107.
[70] *Id.*, at 94, 96.
[71] *Id.*, at 96.
[72] *Id.*, at 33.
[73] *Id.*, at 110. *See also* discussion Appendix A, *infra.* The original moratorium extended for forty-five days. It has since been renewed and EPA has required AGS to find a new test site.

public.[74] Mr. Walter Wong, Director of Environmental Health, Monterey County, California, testified at the hearing that the county felt "the experimental use permit. . . . to conduct a field experiment. . . . was processed in a secretive manner that excluded input from local government and from the public".[75] Mr. Sam Karas, Chairman of the Monterey County Board of Supervisors, testified that, "Prior to the issuance of the permits by EPA or the State Department of Food and Agriculture, no public official in the jurisdiction most affected was notified".[76] Considering that this was to be the world's first authorized deliberate release of a genetically-engineered organism, Mr. Karas continued, "Failure on their part to notify us of an experiment of such national, if not world wide significance, is unconscionable".[77]

Mr. Schatzow agreed that EPA's experience with AGS had increased their sensitivity. "I think the whole question of trying, although again we had difficulties in this case because of the claim of confidentiality, but trying to inform localities and involve local groups is something that we would try to look at in the future if we didn't have a claim of confidentiality." [78]

At the hearing, Dr. Bedbrook testified that,

> *. . . we scientists must work harder to help the public learn more about what we do so that the public can better discern, along with us, the difference between those activities which may present significant risks and those which present only negligible risks, if any . . .*
>
> In addition, the public should be given adequate opportunity to participate in decision making on biotechnology issues. AGS is hopeful that EPA and the other Federal agencies having jurisdiction over biotechnology products will review their procedures to assure that any local communities affected by proposed actions are given early notice and a full opportunity to comment.
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> We also plan to do a better job ourselves of establishing communications with the communities in which we do our field test work.[79] [Emphasis added.]

C. Summary

The "ice-minus" case revealed several factors that are necessary for adequate review by EPA (and others) of proposals to release genetically-engineered organisms into the environment. First, there must be purposeful communication with communities where releases will occur in order to address the concerns of the public in a timely and scientific manner. Second, EPA review of data must be based on mutually defined terms and, with regard to test sites, direct observation when appropriate. Finally, biotechnology companies must endeavor to abide meticulously by research protocols that form the basis for scientific review of products by EPA's Scientific Advisory Panel. Deviations from accepted protocols should be clearly documented and explained. Where the precise parameters of a protocol are in doubt—such as the proper control of a "contained" experiment—companies should seek the advice of the Agency.

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[74] *See,* "Hearing: Ice-minus", *supra,* note 12, Part I, at 104.
[75] *Id.,* at 106.
[76] *Id.,* at 104.
[77] *Id.,* at 104.
[78] *Id.,* at 85–86.
[79] *Id.,* at 7.

CHAPTER THREE: USDA LICENSING OF A GENETICALLY ALTERED VETERINARY VACCINE

On April 29th, 1986, the Investigations and Oversight Subcommittee held a hearing to examine USDA's licensing of a genetically-altered veterinary vaccine for the treatment of pseudorabies.[80] Witnesses at the hearing were as follows:

Dr. Saul Kit, Baylor College of Medicine and Novagene, Inc., accompanied by Gordon Kit, Esquire.

Dr. Michael J. Bartkoski, Jr., Vice President for Operations, Biologics Corporation, Division of TechAmerica Group, Inc.

Dr. Orville G. Bentley, Assistant Secretary for Science and Education, U.S. Department of Agriculture, accompanied by: Mr. Alan Tracy, Acting Assistant Secretary, Marketing and Inspection Services; and Mr. Thomas M. Walsh, Assistant General Counsel, Office of the General Counsel, USDA.

Mr. Jeremy Rifkin, President, Foundation on Economic Trends.

A. Background

In 1982, *Novagene Ltd.* (a general partner of Novagene, Inc.) contracted with the Baylor College of Medicine (BCM) to jointly develop and patent a pseudorabies vaccine.[81] Dr. Saul Kit of BCM, and is also a consultant to *Novagene Ltd.,* was principal investigator in the research.[82]

In early 1983–1984, two pilot studies were performed with the pseudorabies vaccine in BCM laboratories under biosafety levels approved by the NIH Guidelines. On June 26 and 27, 1984, a herd of almost 1,400 pigs (the so-called Maddox herd) was inoculated with the genetically-engineered vaccine to prevent a pseudorabies outbreak. The test was conducted in West Central Texas, under the supervision of Dr. Saul Kit, Dr. Malon Kit, Dr. McConnell of Texas A&M, and Dr. Lawhorn of the Texas Animal Health Commission. The Texas Animal Health Commission, and the National Animal Disease Center, a division of USDA's Agricultural Research Service, were aware of, and participated in the test. The Texas Agricul-

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[80] "Hearing: USDA Licensing", *supra,* note 13, Part I. Pseudorabies is a herpesvirus which infects swine and cattle. In pigs, it is a highly contagious infection. In cattle, it is regularly fatal within two days of the onset of illness. Pseudorabies can be transmitted from pigs to cattle through minute abrasions of the skin. New strains of this virus, which are generally fatal for young pigs, have emerged in Europe and recently in the United States. Figures supplied to Congress by the Animal, Plant Health Inspection Service (APHIS) of the Department of Agriculture show that pseudorabies is responsible for losses of $20 million a year in the swine industry. This figure has remained constant for the past three years. When pigs are identified as having this infection, states may quarantine the herd. Regulations on herd status are more rigorous for breeding herds since this virus is particularly lethal for young pigs. Animals that recover from pseudorabies may continue to harbor a latent form of the virus and can infect other animals.

[81] *Id.,* at 6.

[82] *Id.* (Dr. Kit' son, Dr. Malon Kit, is the President of *Novagene,* Inc.)

tural Extension Service refused to participate.[83] The NIH/RAC and the Institutional Biosafety Committees (IBCs) at Texas A&M and the BCM, were not notified of this field test.[84]

In December 1984, *TechAmerica Group, Inc. (TechAmerica),* by agreement with *Novagene Ltd.* and BCM, submitted an application to USDA to license the pseudorabies vaccine (now called OMNIVAC), under the Virus Serum Toxin Act (VSTA).[85] In April 1985, the Veterinary Services Division of APHIS approved *TechAmerica's* request to conduct field trials of the vaccine in several states. These tests were conducted throughout that summer.

In late October 1985, Veterinary Services officials notified *TechAmerica* and senior officials at APHIS that it had classified the vaccine as a "recombinant organism", and requested certain additional tests be performed to verify the purity and identity of the vaccine.[86] On January 13, 1986, USDA granted *TechAmerica* a license to market OMNIVAC. The Veterinary Services Division did not receive the results from the additional tests it had requested until February 7, 1986. On April 8, 1986, *TechAmerica* voluntarily agreed to suspend sales of OMNIVAC until USDA could publish and document an environmental assessment of the vaccine. USDA released the environmental assessment on April 22 and issued a Finding Of No Significant Impact on the Environment.[87]

The Subcommittee hearing investigated whether the research and field testing of the vaccine had been conducted in accordance with the NIH Guidelines and whether USDA's licensing of the vaccine followed its own laws and guidelines regarding the licensing of genetically-engineered products.

B. Discussion

1. THE NIH GUIDELINES AND THE DEVELOPMENT OF OMNIVAC

The NIH Guidelines require experimenters to notify their local IBCs and the NIH/RAC prior to any deliberate release of an organism containing recombinant DNA molecules. Dr. Kit testified at the hearing that he determined that the field test of the pseudorabies vaccine on the Maddox herd was not subject to the NIH Guidelines because (1) no federal funds were used to develop the pseudorabies vaccine or conduct the test; (2) the pseudorabies vaccine belongs to a category of organisms exempt from the NIH Guidelines; and (3) vaccination of the herd was not a "release into the environment".[88]

a. Federally Funded Research

Dr. Kit testified that the research on the pseudorabies vaccine "was entirely funded by the Houston-based company, *Novagene,*

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[83] *Id.,* at 173, and letter from Dr. Neville Clark, Director Texas Agricultural Extension Service to Subcommittee on Investigations and Oversight, April 28, 1986.

[84] *See* "Hearing: USDA Licensing", *supra,* note 13, Part I, at 290 and 294.

[85] VSTA, 21 U.S.C. 151.

[86] *See* "Shibley letter", appendix F. *infra.*

[87] *Id.,* at 199. USDA's issuance of the Environmental Assessment and *TechAmerica's* voluntary suspension of sales of OMNIVAC were, in part, a response to a lawsuit brought by the Foundation on Economic Trends alleging that USDA failed to follow NEPA requirements in licensing the vaccine.

[88] *Id.,* at 6, et. seq.

Ltd. The development of the vaccine was carried out in my laboratory at the BCM. No federal funds were involved".[89] However, other information provided at the hearing indicates that there was federal support for the vaccine's development. Dr. Kit admitted at the hearing that he had received federal money since 1961 to study herpesvirus and the thymidine kinase (TK) gene.[90] The pseudorabies virus is a member of the herpesvirus family and the TK gene is the gene that Dr. Kit removed from the virus. In addition, the BCM received a substantial share of the patent rights in the vaccine, apparently in return for use of BCM facilities and for the services of a BCM faculty member, Dr. Kit.[91]

In a letter submitted to the Investigations and Oversight Subcommittee, the IBC and BCM took the position that contributions by BCM faculty members subject a research program to the NIH Guidelines. The letter states that, "All research involving recombinant DNA molecules conducted at the Baylor College of Medicine or conducted by Baylor faculty members in their official capacity is subject to the NIH guidelines and Baylor College of Medicine policies." [92] The IBC at BCM notes in the letter that Dr. Kit, in his official capacity as a professor at BCM cosigned the application for the Maddox herd field test filed with the Texas Animal Health Commission. The Commission's letter granting authority to proceed with the trials was addressed to Dr. Kit also in his capacity as a BCM faculty member. From these facts, the BCM concluded tht Dr. Kit was subject to the NIH Guidelines and BCM policies.[93]

b. Applicability of NIH Guideline Exemptions to the Pseudorabies Vaccine

Dr. Kit asserted that the NIH Guidelines specifically exempt experiments with organisms like the pseudorabies vaccine which are altered only through deletion, not addition, of a gene.[94] It is important to note that Dr. Kit did not claim this exemption for his laboratory experiments with the vaccine but rather notified the IBC at BCM of all laboratory experiments with the pseudorabies vaccine prior to the Maddox herd field test.[95]

If research with the pseudorabies vaccine is exempt from the NIH Guidelines, it would not necessarily mean that experiments involving release into the environment would be exempt from review as well. The NIH Guidelines require IBC review and NIH and IBC approval of experiments that involve "deliberate release into the environment of any organism containing recombinant DNA. . . ." [96] The question then is whether the vaccination of the Maddox herd constituted a "release into the environment".

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[89] *Id.*, at 6.
[90] *Id.*, at 150.
[91] *Id.*, at 174.
[92] *Id.*, at 290.
[93] *Id.*, at 291.
[94] Section III-D-2 of the NIH Guidelines exempts from review deletion mutants that "consist entirely of DNA segments of a single non-chromosomal or viral DNA source though one or more of the segments may be a synthetic equivalent."
[95] See "Hearing: USDA Licensing", *supra,* note 13, Part I, at 7.
[96] Section III-A-2 of the NIH Guidelines states; "IF AN EXPERIMENT FALLS INTO BOTH CLASS IIIA AND ONE OF THE OTHER CLASSES, THE RULES PERTAINING TO CLASS IIIA MUST BE FOLLOWED."

c. Vaccination: Release into the Environment?

Dr. Kit testified that vaccination of the Maddox herd was not a "release into the environment". For support, he cited Veterinary Services Memorandum No. 800.68, dated December 4, 1984, which states that: "In normal husbandry and laboratory practices, veterinary biological products are not considered to be a release into the environment." [97]

Dr. Kit defended his position in response to questions from the Subcommittee:

Mr. SENSENBRENNER. . . . Well, you brought up USDA Veterinary Services Memorandum No. 800.68, which states that in normal husbandry and laboratory practices, the veterinary biological products are not to be released into the environment. The memorandum is dated December 4th, 1984, and yet, the Maddox farm field test occurred six months earlier in June of 1984.

Given this, wouldn't the field test have been classified as an environmental release subject to the NIH/RAC approval under the Guidelines in effect at the time?

Dr. KIT. I don't think so. I think that the . . . Veterinary Services Guidelines reflects the thinking of veterinarians, that vaccination under these conditions is not released into the environment. It affirms it.

Mr. SENSENBRENNER. Well, do you or don't you consider the experimental vaccination of 1,300 swine an environmental release?

Dr. KIT. No, I do not.

Mr. SENSENBRENNER. I think that's contradictory, sir, with all due respect.

Dr. KIT. No, sir. If you read the plan, you will see that on this quarantined farm, very careful precautions were taken with regard to where the animals were, with regard to what would happen to them, and how they were disposed of, and so on.

And, again, all of the experiments were done with the knowledge of the experiments already completed at the National Animal Disease Center of the Department of Agriculture, which indicated that there is no shedding.

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Mr. BEDELL. Dr. Kit, you said that there was no environmental release because there was no shedding. Is that correct?

Dr. KIT. That's one reason. There's no environmental release because there's vaccination . . . in a quarantined herd under quarantined conditions.

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Mr. BEDELL. Wasn't . . . part of the test to determine whether or not there was shedding?

Dr. KIT. No, sir . . . this was a—an additional piece of information that could be obtained.

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Mr. BEDELL. But that was part of the purpose of the experiment, was it not?

Dr. KIT. It was already demonstrated by the experiments carried out by Gene Pirtle at Ames, Iowa.

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Mr. BEDELL. My question is: Was part of the test to determine whether or not there was shedding. Either yes or no, it was or it was not. Was part of it to determine it?

Dr. KIT. Yes.

Mr. BEDELL. So if part of it was to determine it, then there was—you didn't know it for sure before you had the experiment or there's no point in having done the experiment.

Dr. KIT. As a scientist, I don't know anything for sure.

Mr. BEDELL. Well, O.K. Then let me read also here: In 1985, TechAmerica wrote letters to the states of Illinois, Michigan, requesting permission to test its vaccine in those States. The letter stated that the tests would be intended to measure the

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[97] "Hearing: USDA Licensing", *supra,* note 13, Part I, at 127-130.

safety of gene-deleted vaccine and that the vaccine virus—would be minimally excreted.[98]

Although Dr. Kit places great reliance on Veterinary Services Memorandum No. 800.68, the memorandum itself leaves open the possibility that a veterinary biological product, such as the pseudorabies vaccine, can be released into the environment:

In the event that a veterinary biological product would be considered to be released into the environment, the issuance of a license or import permit may require an environmental impact statement and interagency approval.[99]

The fact that veterinary biological products can be considered to be released into the environment is further supported by the fact that the IBCs at both BCM and Texas A&M considered the vaccination of the Maddox herd to be a release of the pseudorabies vaccine into the environment. The IBC at BCM summarized its subcommittee's investigation into the Maddox herd inoculation in a letter to the Investigations and Oversight Subcommittee:

The (IBC) Subcommittee found that the inoculation of greater than 1,400 swine at the Maddox farm in central Texas constituted a release into the environment, although the (IBC) subcommittee noted that Dr. Kit had relied on a USDA memorandum to the contrary.[100]

BCM also criticized Dr. Kit's failure to consult with the IBC regarding his interpretation of the NIH Guidelines:

The (IBC) Subcommittee further finds that Dr. Kit should have sought the advice and approval of the (IBC) subcommittee in interpreting NIH Guidelines prior to the initiation of the field test.[101]

The IBC at Texas A&M in a letter to NIH stated:

. . . It is the belief of the IBC that the determination of deliberate release is not the option of the PI (Principal Investigator), and any "potential" release must be evaluated by the IBC, NIH, and RAC reviews.

The investigators have responded by reference to the USDA Veterinary Safety Memorandum No. 800.68 . . .

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In the broad sense of interpretation, this perspective would permit the use of any reconstructed vaccine without evaluation following an "informed determination" that no viral shedding was observed from infected live animals.

The IBC notes that this memorandum was dated after these studies were performed. But more importantly, this memorandum has been interpreted by the PI involved in the pseudorabies studies to prescribe [sic] a very important [sic] exclusory clause to the NIH Guidelines. The TAMU (Texas A&M University) System IBC believes that this memorandum should not pre-empt the Guidelines and such experimentation should be presented for IBC, NIH, and RAC reviews.[102]

NIH is presently investigating whether vaccination of the Maddox herd constituted a release into the environment. The conclusions by the IBCs at both BCM and Texas A&M are critical of the fact that Dr. Kit did not consult with these organizations prior to acting on his determination that his experiments were exempt from the NIH Guidelines.

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[98] *Id.*, at 187.
[99] *Id.*, at 127–30.
[100] *Id.*, at 290.
[101] *Id.*
[102] *Id.*, at 294.

2. USDA REVIEW OF OMNIVAC

At the hearing, the Subcommittee reviewed USDA's licensing of OMNIVAC to determine whether USDA properly reviewed the pseudorabies vaccine in accordance with its policy toward recombinant DNA-derived veterinary biological products.

a. Classification of OMNIVAC

Under the Proposed Coordinated Framework published in December 1984, USDA evaluates veterinary biological products prepared using biotechnology procedures (such as recombinant DNA technology) "individually to determine what will be necessary to establish its purity, safety, potency, and efficacy." [103] The Proposed Coordinated Framework goes on to provide that "additional tests may be required to assure safety, especially when live microorganisms are present in the biological products." [104] Finally, the Proposed Coordinated Framework states that "USDA requires all license applicants or products derived from recombinant DNA technology to comply with the NIH guidelines for research involving recombinant DNA molecules." [105]

In February 1985, two months after *TechAmerica* applied to APHIS for a product license for OMNIVAC, the Veterinary Biologics Staff (VBS) of APHIS' Veterinary Services Division, classified the vaccine as a "Pseudorabies Vaccine, Modified Live Virus, Code 1891.20".[106] The first reference to OMNIVAC as a recombinant DNA-derived product is found in a letter from Dr. Shibley of VBS to *TechAmerica* on November 5, 1985 in which he states that, after the review of the patent's description of the preparation of OMNIVAC, VBS had "no question that it was developed by employing recombinant DNA procedures . . .".[107] Dr. Shibley notified *TechAmerica* that OMNIVAC's production number was now changed to code 1891.RO to identify it as a recombinant organism. Finally, Dr. Shibley stated:

> . . . therefore, . . . in order to avoid any misunderstanding, proper State officials in any state where field trials or experimental work is being conducted should be made aware of the characteristics of this product. *We are advising Veterinary Services and the Animal and Plant Health Inspection Service's Administrator that we are in the process of licensing a recombinant derived modified live pseudorabies vaccine.*[108] [Emphasis added.]

On November 29, 1985, VBS required *TechAmerica* to test that the vaccine was in fact deficient in TK and undertook its own confirmatory testing at the National Veterinary Services Laboratory (NVSL) at the same time.[109]

On January 16, 1986, USDA licensed *TechAmerica* to manufacture OMNIVAC, despite the fact that the results of the tests conducted at the NVSL had not yet been reported to VBS. The results were not known until February 7, 1986.[110] States were not contact-

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[103] 49 Fed. Reg., at 50899.
[104] *Id.*
[105] *Id.*
[106] *Id.*, at 318.
[107] Letter from Dr. George Shibley, Veterinary Biologics Services, to *Biologics Corporation,* November 5, Appendix F, *infra.* (Hereinafter cited as "Shibley letter").
[108] *Id.*
[109] *See* "Hearing: USDA Licensing", *supra,* note 13, part I, at 325.
[110] *Id.*, at 273.

ed until February 4 and 5, 1986. When *TechAmerica* did inform the states that USDA considered the vaccine to be a recombinant organism, *TechAmerica* was able to refer to the vaccine as a licensed product.[111]

The events described above indicate that VBS did not consider the pseudorabies vaccine to be a recombinant organism until it reviewed a product description contained in the patent in late October 1985. USDA disagrees. In response to questions from the Subcommittee, USDA officials assert that the vaccine was always considered to be a recombinant DNA-derived product and that the code change was purely an administrative matter made necessary by a new coding system:

> Materials originally submitted with TechAmerica's license application clearly indicated that the company's product was recombinant derived . . . Recombinant derived products receive an "R" code number to distinguish them from other products. At the time of TechAmerica's application the "R" code system had not yet been developed. . .
>
> There was not actual "reclassification" of the recombinant derived OMNIVAC vaccine. . . The Agency simply applied the new system to OMNIVAC which had received its original code number before the new system was developed.[112]

When asked whether USDA required significant additional tests of OMNIVAC after the November letter changing the code designation of the pseudorabies vaccine, USDA replied:

> Normally, the product reviewer and the Senior Veterinarian, in conjunction with the National Veterinary Services Laboratory, would decide whether additional tests are necessary prior to licensing a product. APHIS was aware of the fact that OMNIVAC was a recombinant-derived product at the time of the original application. Therefore, the change in the product code number had no bearing on the test requirements. However, it should be noted that since this was a recombinant-derived product new test procedures were initiated to characterize the virus, including thymidine kinase assays and restriction endonuclease characterization of the master seed virus.[113]

USDA did not initiate these "new tests procedures" until after the code change in November 1985. In its Environmental Assessment, USDA considered these tests to be necessary to assure the vaccine's safety.[114]

However, when asked why it licensed OMNIVAC before receiving results of these new tests, USDA replied:

> All of the tests required for licensing were completed prior to issuance of the license. The tests referred to in this question provided supplementary, additional data and were not necessary for licensing.[115]

USDA's position that it always considered OMNIVAC to be a recombinant organism is not confirmed by the events chronicled in the correspondence between VBS and *TechAmerica.* USDA did not ask *TechAmerica* to notify the states that the pseudorabies vaccine was a recombinant organism until USDA's letter of November 5, 1985. USDA did not require testing related to the TK deletion until its letter of November 29, 1985. Most importantly, in the letter of

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[111] *Id.*, at 322.
[112] *Id.*, at 304.
[113] *Id.*, at 306.
[114] *Id.*, at 219; "Because the virus was genetically altered, NVSL performed two tests in addition to the tests it normally performs to assure the safety. One test was performed to verify that the virus contained a gene deletion as claimed. The other test confirmed that it was the thymidine kinase gene that was deleted."
[115] *Id.*, at 308.

November 5, Dr. Shibley makes the first reference to the fact that he will advise Veterinary Services Division and APHIS that, ". . . we are in the process of licensing a recombinant derived modified live pseudorabies vaccine." [116]

If USDA, in fact, at the time of *TechAmerica's* application in December 1984, considered OMNIVAC to be a recombinant organism, it is unexplained why USDA waited until November 5, 1985 to require *TechAmerica* to notify the states of the product's nature and to require tests related to the implications of gene deletions. It is also unclear why Veterinary Services within APHIS would need to be "advised" of OMNIVAC's recombinant nature eleven months after *TechAmerica* filed its application and APHIS supposedly, "was aware of the fact that OMNIVAC was a recombinant derived product . . .".[117]

This evidence obtained by the Subcommittee indicates it is more likely USDA did not consider OMNIVAC to be a recombinant organism until late October of 1985. By that time, successful field tests had already been conducted in several states. USDA's request that *TechAmerica* notify the states of OMNIVAC's recombinant nature and its request for tests relating to TK activity appear to have been mere formalities, especially given the fact that USDA licensed OMNIVAC for production before those requests were fulfilled.

b. USDA Procedural Review of OMNIVAC

In July of 1985, the Secretary of Agriculture delegated to the Assistant Secretary of Marketing and Inspection all authority related to regulation of agricultural biotechnology products and delegated all authority over biotechnology research to the Assistant Secretary of Science and Education.[118] Accordingly, *TechAmerica's* application to license OMNIVAC was reviewed by the Veterinary Biologics Staff (VBS), APHIS, a division of Marketing and Inspection.

In correspondence to the Subcommittee, USDA stated that all decisions relating to field testing of OMNIVAC were made by VBS with the support of the National Veterinary Services Laboratory (NVSL) staff, a biometrician from the APHIS Technical Assessment Staff, and a researcher from the National Animal Disease Center.[119] This apparently conformed to APHIS' usual practice:

> Normally, no other agency outside APHIS reviews license applications for animal biologics. However, there are times when other organizations are consulted regarding licensing actions. For example, it is not uncommon to consult with the Food and Safety Inspection Service and the Agriculture Research Service of USDA. Outside organizations such as the Food and Drug Administration and the Communicable Disease Center may also be consulted.[120]

In its Environmental Assessment of OMNIVAC, USDA maintains that the IBCs at *TechAmerica* and Michigan State University reviewed the vaccine's testing and production.[121] USDA also states in the Environmental Assessment that the Agricultural Recombinant DNA Review Committee (ARRC) was "informally kept ad-

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[116] "Shibley letter", Appendix F, *infra.*
[117] *See* "Hearing: USDA Licensing", *supra,* note 13, Part I, at 304.
[118] *Id.,* at 96.
[119] *Id.,* at 306.
[120] *Id.*
[121] *Id.,* at 206.

vised of the license review process" through the efforts of one of the vaccine application reviewers, who is also a member of the ARRC.[122] According to USDA's Environmental Assessment, the APHIS Biotechnology and Environmental Coordinating Staff was kept advised on the licensing process.

At the hearing, Mr. Tracy, Acting Assistant Secretary of Marketing and Inspection testified that the vaccine had gone through "several IBCs, including having gone through our NVSL in Ames prior to submission of the license." [123] Other evidence submitted at the hearing indicates that there was no IBC in existence at the NVSL (or the National Animal Disease Center) until after OMNIVAC was licensed:

> At the time I tested the efficacy of the thymidine kinase negative (tk−) pseudorabies vaccine in swine, there was no Institutional Biosafety Committee (IBC) at the National Animal Disease Center (NADC) dealing with recombinant DNA situations. As a matter of fact, an IBC was only recently appointed by the Center Director. The local IBC is so new that I would not know of its existence if I had not inquired. It thus appears that we at the NADC will have assistance with recombinant DNA guidelines.[124]

This review process is inconsistent with that provided the General Accounting Office (GAO) for their report on the status of biotechnology regulation at USDA.[125] Dr. Shibley of VBS informed the GAO that before licensing a genetically-engineered veterinary biological, APHIS would look closely at the NIH Guidelines, confer with the legal staff at USDA, design an acceptable review procedure, complete with risk analysis for the specific case, seek review by the APHIS biotechnology working group, consult the ARRC and the NIH, and publish the overall request and review process in the Federal Register for comment.[126] When questioned why these procedures were not followed, USDA stated:

> . . . Some of the procedures discussed by Dr. Shibley were not part of APHIS' licensing requirements were simply raised as points of discussion in the agency's effort to review and update its review process.[127]

c. USDA's Substantive Review of OMNIVAC

USDA's substantive review of OMNIVAC is detailed in the Environmental Assessment [128] published April 21, 1986, three months after USDA licensed OMNIVAC. According to USDA, the Environmental Assessment was not prepared and published before licensing of OMNIVAC because, "APHIS did not consider the licensing of OMNIVAC as an agency action of significant environmental impact because of the vaccine's safety and the virus' inability to replicate outside the animal.[129] However, apparently in response to public concern and litigation regarding licensing of OMNIVAC, USDA published the Environmental Assessment "to fully reflect the measures and procedures taken during the licensing process to

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[122] *Id.*
[123] *Id.*, at 247.
[124] *Id.*, at 78, letter to Dr. Kit from Dr. E. C. Pirtle, NADC.
[125] *See* "USDA's Biotechnology Research", *supra,* note 1, Part I.
[126] *Id.*, Background notes.
[127] *See* "Hearing: USDA Licensing", *supra,* note 13, Part I, at 308.
[128] *Id.*, at 199, *et seq.*
[129] *Id.*, at 307.

assure that environmental concerns were addressed, and a Finding of No Significant Impact was published." [130]

The Finding of No Significant Impact contained in the Environmental Assessment is based in part on safety studies conducted by Dr. Saul Kit prior to the *TechAmerica* license application. These studies, "were considered as background information in the licensing process, and provided USDA with a valuable and extensive safety documentation." [131] One of these studies was the test performed on the Maddox herd at Texas A&M.

USDA's reliance on the Maddox herd test—a test which may have taken place in violation of NIH Guidelines—provoked considerable discussion at the hearing. Chairman Volkmer questioned how USDA could ensure that VSTA licensed applicants followed NIH research guidelines:

Mr. TRACY. . . . We do expect that products which would come from recombinant type research . . . would have taken place under the guidelines prior to its having been submitted for licensing under the VST Act, and that was the case with regard to this virus.

Mr. VOLKMER. Wouldn't you require proof that they had followed those guidelines?

Mr. TRACY. We, we have all the backup data that showed that it had gone through several IBCs, including having gone through our own National Vet Services Laboratory in Ames prior to submission of the license. *So it was very clear when we received the application that it had taken place under IBC review* and, therefore—

Mr. VOLKMER. *There have been no IBC review on any field tests.*

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Mr. VOLKMER. My concern is this: Let's assume that reseach is done on a matter, (involving) recombinant DNA . . .

And let's say that whoever has (done the research) get(s) approval before they do the lab tests . . . However, then they go out on their own and do field tests without any approval of anybody. And then they come in and ask for an application—make application to license it, and sell it.

Dr. Tracy, from my understanding of what you have told us just a minute ago, it doesn't make any difference—whether the field tests were done under an approval or disapproval, or no approval.

Mr. TRACY. Well, for the purposes of licensing under the Act, we in effect start the procedure all over. We do our own safety review.[132] [Emphasis added.]

Mr. Tracy further testified that at the time of the Maddox herd field test, USDA had no authority to regulate the intrastate shipment of the pseudorabies vaccine:

Mr. TRACY. Mr. Chairman, *we did review in APHIS all of the field tests that took place after the time of . . . license application . . .*

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Mr. VOLKMER. *What about field tests that take place before?*

Mr. TRACY. *Those which were taken place intrastate, we had at that time no authority to require . . .* permission. We now have that authority and we expect to take advantage of that authority for development of new regulations. But we have a very strong body of regulation in place.

Mr. VOLKMER. It's amusing to me that EPA tells AGS that they can't do what they tried to do in California—and that's all in California. But you tell me you can't do anything and it's all in Texas where the matter is taking place—until we pass a law saying you can.

Mr. TRACY. . . . USDA had no jurisdiction at—under the Virus Serum Toxin Act, for intrastate movement of that virus at that time. That has since been corrected by

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[130] *Id.*

[131] *Id.* at 199, *et. seq.*

[132] *Id.*, at 248.

Congress and will be finalized through issuance of formal regulations.[133] [Emphasis added.]

USDA's position that it could not monitor NIH Guideline compliance by license applicants, because it had no intrastate regulatory authority at the time led to the following exchange between Mr. Bedell and Mr. Tracy:

Mr. BEDELL. *I don't understand why you need any authority. You are going to license them, depending upon whether or not you feel those tests are satisfactorily carried out or not, aren't you? . . . And if they were not satisfactory, you don't need any authority, you just don't license them.* I don't understand.

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Mr. TRACY. We have no basis to say that any tests were improperly conducted.

Mr. BEDELL. And you don't think it's up to you to look at that, and determine that?

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You see, this case isn't the issue. The worry we have is that in the future we may release things that shouldn't be released, and apparently you don't think that's your worry.

Mr. TRACY. Now, we're talking about two separate items here. The tests were part of the research which was taking place under Guidelines. . .

Mr. BEDELL. Wait a minute. Supposedly taking place under Guidelines.

Mr. TRACY. . . . (A)ll tests that have taken place before, no matter who approved them, would be things that we would look at and try to determine whether the product is safe.

Mr. BEDELL. *But the Act requires, does it not, compliance with NIH Guidelines?* Is that right?

Mr. TRACY. *The Act in and of itself does not require compliance with NIH Guidelines. We do have a Policy Statement* that was published in the Federal Register in 1984—December 31—*which says that USDA requires all licensed applicants for products derived from DNA technology to comply with NIH Guidelines* for research involving recombinant DNA molecules.

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Mr. BEDELL. *But your regulations require compliance with NIH Guidelines.* Is that correct or incorrect?

Mr. TRACY. *No. We have a Policy Statement——*

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Mr. BEDELL. But . . . *if you require somebody to do something, then you must have to satisfy yourself that they have done that. How do you satisfy yourself that that's been done?*

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Mr. TRACY. I'm sorry. *I, perhaps, spoke too strongly by using the word 'required' then.* We——

Mr. BEDELL. Well . . . Do you require it or don't you require it?

Mr. TRACY. *We expect them to do it* and we do not have any formalized review procedure to ensure that they have. We do, however, have plenty of opportunity to see what was done. And it is pretty apparent when you look at the tremendous body of—of work done here that this was reviewed under NIH Guidelines.

Mr. BEDELL. So you do not require it, apparently. You would like to have it done but you don't require it.

Mr. TRACY. I will correct my original earlier statement and agree with you, sir.

Mr. BEDELL. . . . If that's the case, I think this is a terrible deficiency.[134] [Emphasis added.]

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[133] *Id.*, at 252.

[134] *Id.*, at 252–255.

C. Summary

As in the case of "ice-minus", USDA's licensing of OMNIVAC shows the problems researchers and federal agencies can encounter in following and implementing guidelines concerning biotechnology products. Not only did USDA needlessly delay identifying the vaccine as a "recombinant organism" but the principal investigator, Dr. Kit, failed to confirm his interpretation of the NIH Guidelines with the local IBCs or with the agencies themselves. USDA's inability to regulate intrastate shipments under the VSTA prior to 1986 was exacerbated by the absence of a clear USDA policy toward the use, in VSTA license applications, of data obtained from tests conducted outside the NIH Guidelines for recombinant DNA research.[135] Finally, USDA's tardiness in following its own procedures for review of biotechnology products unnecessarily delayed the marketing of the vaccine after it was proven to be safe.

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[135] Although USDA's December 1984 policy statement stated that applicants for a VSTA license are *required* to follow the NIH Guidelines, it appears that USDA had no means of monitoring or enforcing the requirement at the time OMNIVAC was field tested in 1984. USDA's 1986 policy statement *recommends* compliance with the NIH Guidelines. In subsequent correspondence with the Subcommittee, USDA stated that data from tests not conducted in compliance with the NIH Guidelines will not be accepted in support of VSTA license applications. (*See* "Hearing: Coordinated Framework", *supra,* note 14, Part I, at Appendix 6.)

PART III

ISSUES RELATED TO THE FEDERAL COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY

On June 26, 1986, the Administration finalized and published a Coordinated Framework for Regulation of Biotechnology.[1] As did its predecessor, the Coordinated Framework distributes regulatory jurisdiction over biotechnology research and products among various federal agencies on the basis of existing statutory authority. Partly in response to problems associated with review of planned releases under the Proposed Coordinated Framework, the Coordinated Framework attempts to clarify which organisms are subject to which levels of review and to promote comparably rigorous standards of review from agency to agency.

The Coordinated Framework will bear the full burden of determining whether new genetically-engineered organisms can be released safely into the environment. This Part of the report first discusses the hearing at which the Coordinated Framework was examined. It then analyzes the definitions, jurisdiction, and authority relied upon by the Administration for the regulation of biotechnology.

[1] 51 Fed. Reg. 23302.

CHAPTER ONE: COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY

On July 23, 1986, the Investigations and Oversight Subcommittee in conjunction with the Natural Resources, Agriculture Research and Environment Subcommittee and the Science Research and Technology Subcommittee held a hearing to examine the Coordinated Framework and its planned implementation.[2]

Witnesses at the hearing were as follows:

Dr. David Kingsbury, Chairman, Biotechnology Science Coordinating Committee, Office of Science and Technology Policy.

Dr. Monica Riley, Chairman, Committee on Genetic and Molecular Microbiology of the Public and Scientific Affairs Board, American Society for Microbiology, and Professor, State University of New York at Stony Brook.

Dr. Margaret Mellon, Director, Toxics Program, Environmental Law Institute.

Dr. Elliott A. Norse, Ecological Society of America.

Dr. Jack Moore, Assistant Administrator for Pesticides and Toxic Substances, U.S. Environmental Protection Agency.

Dr. Orville Bentley, Assistant Administrator for Science and Education, U.S. Department of Agriculture.

Karen Darling, Deputy Assistant Secretary for Marketing and Inspection, U.S. Department of Agriculture.

Mr. Richard Godown, Industrial Biotechnology Association.

A. Development of the Coordinated Framework: Role of the Biotechnology Science Coordinating Committee

The Coordinated Framework was compiled by the Domestic Policy Council Working Group on Biotechnology, which had been charged with the difficult task of bringing together the diverse views and expertise of the various agencies into a comprehensive regulatory system for biotechnology. The DPC Working Group deferred certain science questions to the BSCC. Because all members of the BSCC are also members of the DPC Working Group, Congressman Volkmer asked Dr. Kingsbury, Chairman of the BSCC to explain its relationship to the DPC Working Group. Dr. Kingsbury replied, "The BSCC has been dealing with questions strictly related to science . . . the DPC working group . . . is a very broad group that has active participation by all of the (18) represented agencies and not just the five agencies . . ." [3] Mr. Volkmer then asked:

Mr. Volkmer. Well, is it policy or coordination of just pure science? In your statement, you say, "The BSCC will continue to have the primary responsibility for the scientific questions that arise in the future, including questions associated with risk assessment methodology and its further development and implementation."

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[2] "Hearing: Coordinated Framework", *supra,* note 14, Part I.

[3] *Id.,* at 30.

Dr. KINGSBURY. *We consider that a question of science. We're talking about risk assessment methodology, not risk management methodology.* We have dissociated those two and continue to dissociate them. *That risk assessment is a scientific undertaking that does not--that provides the basis on which to make risk management decisions.* And as I pointed out in here, the BSCC is not involved in questions of risk management; it's simply risk assessment methodology.[4] [Emphasis added.]

Dr. Kingsbury further testified that the BSCC would "regularly review the appropriateness of the scientific basis of existing regulations" and would make "recommendations to modify existing statutes, if it is deemed necessary." [5] Mr. Volkmer then queried, "Is that policy or science?" [6]

Dr. KINGSBURY. Those would be recommendations based on science.

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We will be assessing the technology as it is being developed. We will see the direction that new products are going. Remember that one role that the BSCC is playing is to participate in discussions regarding new kinds of product applications that come into the agency and the means whereby the agencies feel it's appropriate for them to handle those, so that there will be discussion of specific applications and of questions that have arisen during review of specific applications.

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We then will be able to recommend . . . how those should be regulated, (and) be reviewed. Now, whether it's the BSCC who comes forward with the recommendation or whether it's the agencies, I think that is a good question.[7]

There was general agreement at the hearing that the DPC Working Group and the BSCC had done a good job at admittedly difficult tasks. The Coordinated Framework is noteworthy in that it coordinates in a comprehensive manner the regulation of commercial and research products of biotechnology at an earlier stage than has been the case with the regulation of other developing technologies.

The Subcommittee was also concerned with the nature of the BSCC's interaction with the various agencies, specifically whether the BSCC would perform a review function similar to that engaged in by the Office of Management and Budget (OMB):

Mr. VOLKMER. But what concerns me is, let's say that Dr. Moore . . . (at) EPA or the Assistant Secretary (of USDA) . . . in reviewing FIFRA or TSCA, decides that, "Hey, we need a minor change or we need this little paragraph changed within the law." Can they come to the Congress or do they have to go through you first before anybody can say it?

Dr. KINGSBURY. Those are agency responsibilities and it's not the responsibility of the BSCC to be the clearinghouse. We believe that such questions would be discussed in the BSCC and the BSCC might make a recommendation. But we do not have the force of absolutely setting down the standard of how EPA does its business. EPA is an agency that has statutory responsibility to do that business, and that's the only way that they can fully proceed.[8]

Dr. Kingsbury specifically confirmed that the BSCC would have no formal or informal contacts with OMB regarding agencies' proposed rules.[9]

Both Rep. Schneider and Rep. Volkmer expressed concern over the dearth of research in risk assessment compared to product de-

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[4] *Id.*, at 30-31.
[5] *Id.*, at 22.
[6] *Id.*, at 31-32.
[7] *Id.*, at 32.
[8] *Id.*, at 32-33.
[9] *Id.*, at 35.

velopment research. Dr. Kingsbury felt the BSCC should not directly affect biotechnology research priorities:

. . . those research priorities must be set by the research agencies and not by a central committee. We can encourage those agencies, we can have broad discussions between various members of the research agencies, but I feel that we can point those questions out. I am really reluctant to put the BSCC in the position of trying to set for the individual research funding agencies their priorities.[10]

Rep. Schneider queried whether a user fee system was contemplated for the review of biotechnology applications:

Miss SCHNEIDER. . . . Does the administration have a position on user fees for biotech application?

Dr. KINGSBURY. That is not something that we have discussed in detail. The discussions that have come up around user fees have been in the context of the Food and Drug Administration. Commissioner Young has testified regarding his attitude of the implementation of user fees. That has not been an issue that either the Domestic Policy Council Working Group or the BSCC has addressed.

Miss SCHNEIDER. Are you going to?

Dr. KINGSBURY. It is not currently on our agenda. It may come to our agenda. But it is not something that currently is on our agenda.

Miss SCHNEIDER. Well, I am interested in it from the fiscal point of view also, because the Department of Agriculture indicated that they were not interested in spending any more than $5,000 on an impact assessment, and I think that we have to sort of weigh where we're going to be spending those moneys, where they are anticipated coming from, et cetera.

Dr. KINGSBURY. Well, this is an issue that is extraordinarily complex, and while I have spoken with Commissioner Young about his philosophy, which I find, when he explains it, compelling, one concern that has been expressed by the industrial people is that in many cases some of the companies that are involved with some of these new products, especially in the plant sciences, are smaller companies, and the implementation of a significant user fee clearly impacts the smaller companies more than it does the Fortune 500.

That has been a concern, so we are trying to balance—I think the notion has been to balance that. Again, this is not an issue that we have dealt with.

Miss SCHNEIDER. Well, I think that that certainly makes good sense, and so when you are dealing with this issue, I hope you will keep in mind that, yes, there are very small companies that are involved in this type of business as a business, essentially. But also I sure would not like to be on this committee when we do have a problem and find out that the Environmental Protection Agency did not do an assessment because they could not afford to do it, and so therefore, the public welfare was not being protected.

So I think that if that is to be the case, then certainly you, among others, are going to have to come before Congress and say, "Congress, you must reorient your priorities and make sure that we have adequate funding for the Environmental Protection Agency, for NIH or the Department of Agriculture or whomever, so that we can, you know, implement our duty."

Dr. KINGSBURY. I understand.[11]

Although the BSCC, as an interagency coordinating committee, has no regualtory authority, it was still criticized for adopting a "coordinating" style laden with regulatory impact. Dr. Margaret Mellon of the Environmental Law Institute testified:

Where a new technology impacts the territory of several major agencies, coordination is a legitimate and a needed function, but where an agency, without authority sets about coordinating agencies with substantial authority, there can arise a temptation to impose positions on the coordinated agencies, often in the name of consistency. This temptation should be avoided.

In matters that have regulatory significance, the imposition by the BSCC of its position on member agencies could constitute an improper usurpation of authority. Such usurpation is of special concern because of the BSCC's tendency to meet and

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[10] *Id.*, at 31.
[11] *Id.*, at 28-29.

reach its decisions behind closed doors without keeping adequate records of its deliberations.[12]

As for its future role, the BSCC has established five working group subcommittees to examine issues of risk assessment; greenhouse containment standards and definitions of containment and release; training; research and research needs; and public information and education.[13]

The subcommittee on containment standards and definitions of containment and release received the most attention at the hearing, primarily for what it had not yet accomplished. At the hearing, Mr. Scheuer expressed his concern that the subcommittee on release and containment had met only one time to discuss the vital issue of what constituted a "release".[14] Dr. Kingsbury responded by saying that the BSCC itself had only been in existence about nine months and for most of that time had occupied itself dealing with the scientific questions coming before the Committee.[15]

The issue of what is a release was central to two hearings held by the Investigations & Oversight Subcommittee this year.[16] Dr. Kingsbury felt that the definition of "contained" found in EPA's document was a very conservative one, and while it was considered a "working definition," a place to start, it was functional.[17]

When asked what the BSCC could do to ensure that the agencies' policies remained coordinated during the promulgation of different rules, Dr. Kingsbury replied,

> It is our intention that the scientific questions associated with any rulemaking will be discussed with the BSCC. In addition, it is the role of the Domestic Policy Council Working Group on Biotechnology to continue to monitor and coordinate the various agency statements and rulemaking.[18]

Mr. Volkmer also inquired what role the BSCC would have in ensuring that reviews by different agencies of applications to release genetically-engineered organisms would be of comparable rigor.

> Dr. KINGSBURY. . . . it is the intent of the BSCC to monitor the progress of various applications and to review the nature of the applications and of the review process. Where appropriate we will encourage the sharing of staff between the agencies. This review process will allow each agency to understand the nature of the reviews done by the other agencies and to adopt those elements which might strengthen their review process. We have no statutory authority to demand that an agency follow a prescribed procedure but the force of peer pressure by the other members of the committee will assist in encouraging agency adoption of appropriate review procedures.[19]

B. DEFINITIONS

The Coordinated Framework defines those genetically-engineered organisms subject to review, and the applicable standards of review to be applied. Some witnesses criticized the BSCC for developing these definitions with little formal input from ecologists and groups

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[12] *Id.*, at 46. *See also,* discussion, *infra,* Part III, at 49–50.
[13] *Id.*, at 20.
[14] *Id.*, at 39.
[15] *Id.*, at 40.
[16] *See* discussion, *supra,* Part II, Chapters Two and Three.
[17] *See* "Hearing: Coordinated Framework", *supra,* note 14, Part I, at 41. *See also,* 51 Fed. Reg. at 23335.
[18] "Hearing: Coordinated Framework", *supra,* note 14, Part I, at Appendix 1.
[19] *Id.*

outside the agencies. Dr. Elliott Norse of the Ecological Society of America expressed the following concern:

Dr. NORSE. *The preamble seems to reflect the views of genetic engineers, not those of ecologists.* Although the BSCC recently stated that it sought input from scientific societies, it never contacted ESA (Ecological Society of America). *Given the central role of ecology in this issue, that seems to be a serious omission.* Unfortunately, the framework clearly reflects the absence of our input.[20] [Emphasis added.]

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Dr. KINGSBURY. . . . There is a cautionary note that I would like to . . . throw out, and that is that there is a tendency to focus attention, by people who look at the framework, at the preamble. Now, I think that all of us in Washington who deal with these giant documents that come flowing across our desks have fallen into the trap of only reading the executive summary, only to discover that soon someone is asking us about something that was embedded in chapter 7 which we never managed to get to. I think that the same—the same principle applies here.

The executive summary of the statement was really an overview, and we have tried to caution people that to get the detailed and intricate information that really is part of the policies, one needs to read the policies from each of the agencies. I think that a reflection of that is the notion as to what is really involved in the review of microorganisms. As I pointed out earlier, the EPA document, in their summary table, very clearly lines out the fact that there are no classes of organisms, microorganisms, that are not reviewed; it's simply the nature of the review.

I think we must keep that kind of perspective as we go on to these discussions. There are not things that are completely out of the regulatory matrix, but it's a question of the regulatory approach . . . that is being taken.

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Mr. VOLKMER. . . . No ecologists, is that correct, were involved in the development of the guidelines?

Dr. KINGSBURY. I think that that may be a bit of an oversimplification in the sense of the breadth of the process of agency review that went on. The agency positions were developed through broad discussions with their advisory committees, their committee structure.

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I believe that there is, at different levels of agency activity, representation of a variety of scientific specialties. *Within the BSCC itself, you are absolutely right, there are no ecologists sitting on that committee. There are people who represent the ecological research environment,* in the cases of Dr. Ehreth; certainly the R&D activity at the EPA is a reflection, to a great extent, of that kind of activity. Certainly, NSF is involved in that. I won't claim to represent the ecologists in that context, but certainly we have input from them.

So it's a question of agency-level participation versus coordinating committee participation.[21] [Emphasis added.]

Mr. Volkmer then asked whether, in practical terms, only the BSCC members created the definitions.

Mr. VOLKMER. Well, then you're saying—well, let me put it this way. The definitions as to what should be subject to review and how much review, was determined by the BSCC.

Dr. KINGSBURY. No, not that—that's not strictly true. The BSCC, as was pointed out, has no statutory responsibility.

Mr. VOLKMER. That's right.

Dr. KINGSBURY. So it has no direct definitions that it applies to anything. It worked with the agencies, to assist the agencies in getting consistency within their definitions. The definitions that go into place are those in the agency statements. The agencies worked with their advisory committees as they derived what they believed were appropriate statements. They worked with the BSCC in the derivation of what is an appropriate common statement, so that there was consistency.[22]

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[20] *Id.*, at 74.
[21] *Id.*, at 83–84.
[22] *Id.*, at 84–85.

This process was criticized by Dr. Mellon who found no authority in BSCC to determine the scope of regulatory statutes:

Dr. MELLON. . . . Although scientific in content, these [definitions] are purely regulatory in impact. Especially in the case of USDA and EPA, *these definitions determine the scope of regulation under existing statutes.* Defining the scope of statutory authority is properly the function of the agency charged by Congress with the administration of the statute.[23] [Emphasis added.]

The Coordinated Framework distinguishes between the risks posed by different categories of genetically-engineered organisms. "Intergeneric" organisms are considered potentially more dangerous than "intrageneric" ones. The Coordinated Framework defines an "intergeneric organism" to be, "those organisms deliberately formed to contain an intergeneric combination of genetic material." [24] All other organisms are considered *intra*generic. However, excluded from the definition of "intergeneric organisms" are those organisms that result from the addition of intergeneric material that is well characterized and contains only noncoding regulatory sequences.[25] This exclusion caused the greatest amount of concern among the scientists at the hearing.

Dr. Monica Riley, in testimony prepared by the Public and Scientific Affairs Board of the American Society for Microbiology, said:

Dr. RILEY. . . . *First, we do not favor exemption of intergeneric hybrids that contain only regulatory sequences in the introduced DNA.*

. . . *we believe that there should be no distinction made between the level of review afforded to noncoding and to coding sequences.* The reason for this is: Although in most cases . . . a foreign regulatory sequence will be entirely innocuous, still one must take into account the fact that some regulatory sequences have the capability to increase the expression of the associated gene very many-fold. Also, regulatory sequences carry specificity determinants which govern when a gene is turned "on" and "off" in response to chemically specific signals.

Although, it is true that regulatory sequences do not affect the composition of the gene product in any way, there is the possibility of major quantitative changes in the amount of gene product produced and changes in the signal which would turn the gene "on" that could possibly in some cases cause problems.[26] [Emphasis added.]

Dr. NORSE. *Altering regulatory sequences and deleting genes can affect an organisms' survival, reproduction, and have environmental effects.* I surmise that the rationale for exempting these alterations is that if no sequences coding for proteins are modified, changes will be merely quantitative and, hence, minor.

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Regulatory sequences that change growth and reproductive rates by just a few percent could dramatically alter competitive balances among organisms in nature.[27] [Emphasis added.]

The Coordinated Framework places a regulatory emphasis on pathogens by subjecting organisms containing genetic material from a non-pathogenic source organism to a lesser standard of review. Dr. Norse took exception to this distinction at the hearing.

Dr. NORSE. The preamble's focus on pathogens also reveals a poor understanding of ecology. If the aim is to avoid adverse environmental effects, we also need to examine organisms' other interactions, including predation, parasitism, competition,

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[23] *Id.,* at 46. The BSCC-recommended definitions are being adopted by the respective agencies in accordance with proper procedures. If any of the affected agencies chooses to modify the definitions, it would appear to be within its power.

[24] 51 Fed. Reg., at 23307

[25] While regulatory sequences do not encode specific proteins, they are in fact the signals which determine which genes are expressed and what amount of a specific gene product is produced.

[26] "Hearing: Coordinated Framework", *supra,* note 14, Part I, at 60.

[27] *Id.,* at 75.

and mutualism. *The focus on pathogens suggests that those who drafted the framework have the narrow view of life peculiar to those in human-centered biological disciplines: that either organisms are pathogens, or that they can safely be ignored.* In fact, the species eliminated by a competitor, a predator, or a parasite is just as extinct as one eliminated by a pathogen. The input of ecologists would have helped BSCC to appreciate this.[28] [Emphasis added.]

In contrast, Dr. Riley felt the accent on regulating pathogens was well placed:

Dr. RILEY. *Concerning simple mutants with no genetic exchange,* we make a distinction between nonpathogens and pathogens. First of all, concerning simple mutants of nonpathogens. *We support the proposal in the guidelines to exempt them from regulation.*

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But as far as pathogens go, in contrast, we support the proposal that all pathogens and their derivatives, no matter what the alteration, should be scrutinized before being introduced into the environment.

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In summary, the answer to this question, with the exception of the exemption of intergeneric regulatory sequences, we support the formulations of categories of organisms demed to pose sufficient risks to warrant being scrutinized for the need of regulation before their deployment.[29] [Emphasis added.]

C. EPA

Under the Coordinated Framework, EPA will regulate the environmental release of microbial pesticides under FIFRA and the release of all other genetically-engineered microorganisms under TSCA.

As explained by Dr. John Moore, EPA's Assistant Administrator for Pesticides and Toxic Substances:

Dr. MOORE. . . . *we have tried . . . to tailor the level of review to the nature of the change that was effected using biotechnology, and the degree of risk that may possibly be associated with the use of that material.*

The agency's conclusion is that there are primarily three categories of microorganisms that currently deserve the closest regulatory attention . . . microorganisms with new characteristics or that are new to the environment in which it is proposed to be used; *microorganisms that have hazardous components* in them, either they are pathogenic or received something from a pathogenic organism; *or, third, microoganisms that are used in the environment*—and . . . *therefore have the potential for widespread exposure.*[30] [Emphasis added.]

In correspondence with the Subcommittee, Dr. Moore defended the agencies' decision to regulate pathogens as well as intergeneric combinations of organisms:

The Agency's decision is based on extensive consideration of the current state of science. EPA consulted persons who are experts in the fields of microbiology, molecular biology, ecology, and taxonomy. These experts came from within the federal government, from the academic sector, and from industry. Some of these experts are members of the society for which Dr. Norse was testifying—the Ecological Society of America. These scientists' comments suggested that there is a wide range of opinion among scientists as to the nature, magnitude, and likelihood of risks that may occur with genetically-engineered (and other) microorganisms. Most of the scientists indicated that EPA's choice to focus particular attention on pathogens and inter-generic microorganisms is a reasonable way of integrating the uncertain and rapidly developing science with the statutory requirements.[31]

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[28] *Id.*
[29] *Id.*, at 60–61.
[30] *Id.*, at 96–97.
[31] *Id.*, at Appendix 5.

1. TSCA

TSCA gives EPA broad authority to regulate organic or inorganic "chemical substances" including microorganisms.[32] EPA believes this authority can be used to regulate recombinant DNA products as well.

Under TSCA, EPA plans to regulate genetically-engineered organisms in the following ways:

(1) Premanufacture Notification (PMN)—the manufacturer of any microorganism that has been deliberately altered to contain genetic material from different genera must submit a PMN for the "new" substance. This requirement is presently in effect.[33]

(2) Significant New Uses of Microorganisms—EPA may promulgate rules to regulate significant new uses of existing chemical substances. Under the Coordinated Framework, EPA intends to define introduction of pathogenic microorganisms into the environment in any amount as a "significant new use" requiring notification to EPA. Until promulgation of a "significant new use" rule (SNUR), EPA is requesting voluntary compliance with this policy.[34]

(3) Reporting rule—TSCA authorizes EPA to issue rules requiring manufacturers, importers and processors of specified chemical substances to submit production and exposure information to the Agency. EPA plans to collect this information prior to environmental release of those microorganisms that are subject to TSCA, but that are not subject to PMN or SNUR notification requirements. The types of information that companies will be required to submit will be developed and established through rulemaking.[35]

(4) Substantial risk reporting—TSCA requires all manufacturers, processors, and distributors of microbial products subject to TSCA, including those involved in research and development (R&D) to report substantial risks posed by such products under Section 8(a) of TSCA. This is immediately effective.[36]

(5) Research and Development (R&D) exemption—TSCA exempts from PMN and SNUR notification requirements chemical substances manufactured in small quantities used solely for R&D. EPA plans to amend these rules to specify that field testing of microorganisms does not fall within the definition of "small quantities for R&D." Until that time, EPA expects submitters to comply with this policy voluntarily.[37]

(6) Exemption from PMN requirements—TSCA allows EPA to exempt from PMN requirements chemical substances it finds will not present unreasonable risks. EPA believes that closed-system uses of new microorganisms will often present lower risks than environmental releases of the same organisms. They are presently awaiting further public comment to determine if such an exemption is feasible.[38]

Dr. Riley expressed concern about TSCA's use to regulate biotechnology products:

Dr. RILEY. . . . We have not been persuaded that TSCA is an appropriate vehicle for regulating the introduction of altered organisms. The definition of genetically altered microorganisms as "new chemicals" is strained. Existing procedures for the control of toxic chemicals do not apply easily to the control of living microorganisms. It appears that it will be necessary for a new set of rules to be developed in order to be able, appropriately, to regulate living microorganisms under TSCA.[39]

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Mr. VOLKMER. . . . I think some of us again that are laymen, in looking at this, realize that TSCA was developed for a chemical industry which is a lot different from a biotechnology industry where you're going to have possible microbial bacteri-

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[32] *See* TSCA, *supra,* note 36,, Part I.
[33] 51 Fed. Reg. at 23325 and 23327.
[34] *Id.,* at 23328.
[35] *Id.,* at 23321.
[36] *Id.*
[37] *Id.,* at 23330.
[38] *Id.,* at 23332.
[39] "Hearing: Coordinated Framework", *supra,* note 14, Part I, at 59.

ological uses that have different traits than chemicals. That's what I think concerns some of us.[40]

Mr. Volkmer questioned whether EPA's definitions for "new" and "existing" were workable:

Mr. VOLKMER. Now, under TSCA, EPA has defined intergeneric organisms as "new" substances subject to premanufacturing notification requirements, and all other organisms as "existing" organisms not subject to such requirements. Is this distinction workable and scientifically valid? Dr. Riley?

Dr. RILEY. In the main, I think, yes, although it grates a little on the nerves of some scientists to characterize a living organism as a new substance in the same category as new toxic chemicals. So it bothers us a little in the sense that that's not the way you would define it if you were starting from scratch.

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But in view of the fact that these people are working with an existing statute and with TSCA, I think that they've done the best that could be done.[41]

Further clarification of how TSCA will be applied to biotechnology products was provided by Dr. Moore.

Mr. VOLKMER. Now, if EPA allows the release of an intergeneric pathogen, let's say, on one acre of land in Florida or any place else, the organism goes on the inventory and anyone can release it anywhere unless EPA adopts a significant-new-use rule that requires notification before using it again elsewhere, like 400 acres in my district in Missouri, and 10,000 acres in Kansas. Is that correct?

Dr. MOORE. . . .Unless we made some type of restriction at the time we allowed something to go on the inventory, once it is on the inventory, it is totally unrestricted. Our intent would be, I think, early on, to work under a presumption that indeed we likely will . . . subject it to SNUR to make sure other people can't do things we're preventing the original requester to do—or something similar to that, some type of a restricted inventory category. . .[42]

Mr. Volkmer questioned whether EPA could regulate environmental releases of existing organisms before promulgation of the new rules.

Mr. VOLKMER. . . . Now, prior to the promulgation of your significant-new-use rule, and that is going to be probably, what, 9, 10 months, maybe a year before we have that in place?

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How do you learn of releases into the environment of existing organisms?

Dr. MOORE. Congressman, as we sit here today, with the exception of an individual who may be at the stage of feeling that they want to commence commercial manufacture of an organism, anything that they must do that might fall under the purview of TSCA has to be done on a voluntary basis.

Mr. VOLKMER. And if they don't do it, there is no violation?

Dr. MOORE. Correct.[43]

Thus, because of the exemptions for research and development activities and for small businesses, EPA has little authority under TSCA to review environmental releases of genetically-engineered microorganisms until promulgation of new rules. Even then, some non-pathogenic organisms and organisms combining intrageneric genetic material will receive only abbreviated review.[44]

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[40] *Id.*, at 133.
[41] *Id.*, at 92.
[42] *Id.*, at 133–134.
[43] *Id.*, at 130–131.
[44] Manufacturers of these "low risk" organisms are still subject to the requirement of reporting "significant risks" under TSCA Section 8(e) and reporting production and exposure under Section 8(a).

Dr. Mellon expressed the difficulties with applying TSCA to biotechnology products.

Dr. MELLON. If vigorously implemented, Section 8(a) (reporting) is probably adequate for monitoring activities involving engineered organisms. But I believe it could prove an inadequate mechansim for responding to problem releases identified through the monitoring process. Problems might arise in the following situation. What if EPA receives 8(a) notice of an *intrageneric* organism about which it has concerns and would like to restrict the dissemination of the organism pending the development of more information. What recourse does the agency have? If the organism is not regulated under Section 5 of TSCA (PMN and SNUR), the only way to regulate organisms is under existing chemical or imminent hazard provisions of the statute. These provisions are procedurally so burdensome that the agency will find it impractical, except in egregious cases, to follow up on the leads the 8(a) notices provide.[45] [Emphasis added.]

Mr. Volkmer questioned what other gaps in TSCA EPA would need to fill to regulate biotechnology:

Mr. VOLKMER. Now, you correct me if I am wrong, but presently under TSCA, substances used for research and development, not for commercial use, are exempt from premanufacturing notification and significant-new-use reporting. Is that correct? [46]

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Dr. MOORE. Right. Congressman, a company that is not deriving any funds from a Federal source and therefore not be impacted by the NIH Guidelines or USDA Guidelines or something like that, as it sits right now, if they were totally non-commercial and it was non-pesticidal in nature, they would be exempt.[47]

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Mr. VOLKMER. How are you planning to address this problem?

Dr. MOORE. That is one of the rulemakings that we are working on to make organisms subject to reporting and not be under the R&D exemption that currently exists.

Mr. VOLKMER. Do you have sufficient statutory authority to do that?

Dr. MOORE. We're reasonably comfortable that TSCA can get into that.[48]

Dr. Moore also discussed whether EPA could regulate non-federally funded *non-commercial* research and development under TSCA:

. . . Section 5(i) of TSCA exempts non-commercial research and development from section 5 of TSCA. Therefore, non-commercial research with microorganisms is not subject to either premanufacture notification or significant new use notification requirements, as both of these are section 5 requirements.

Non-commercial research is not exempt from section 8 of TSCA, however. Thus EPA may require reporting of environmental releases involving non-commercial uses of microbes using the section 8(a) reporting requirement. This issue will be addressed during the course of the 8(a) rulemaking.[49]

Similarly, EPA has found it necessary to re-define "small manufacturer" in the context of the biotechnology industry. EPA is currently developing a proposed rule which it expects to publish in the *Federal Register* in the Spring of 1987.[50]

Certain data is vital to the risk assessment process when dealing with microorganisms. Questions regarding the ability of EPA to

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[45] Hearing: Coordinated Framework", *supra,* note 14, Part I, at Appendix 3.
[46] *Id.,* at 131.
[47] *Id.,* at 132.
[48] *Id.,* at 131.
[49] *Id.,* at Appendix 5.
[50] *Id.*

collect that data prompted the following exchange between Mr. Volkmer and Dr. Moore.

Mr. VOLKMER. Now, OSTP recently commissioned a report on risk assessment methods for biotechnology. It stated in the report that an important requirement in the risk assessment process is detailed knowledge of the environmental and pathogenic characteristics of the modified microorganisms.

Now, will the premanufacturing notice or 8(a) reporting requirements address this?

Dr. MOORE. We would hope so. We may have to go about it indirectly. Let me take a minute to explain what I mean by that. TSCA is written to not require data upfront to be in the same envelope as the request for consideration to be added to the inventory.

I think what the agency plans to do is to identify the types of information it thinks is required in order to make as an informed judgment. If indeed the regulated industry doesn't listen to what that is, or fails to heed what I think is reasonable recommendations, we would then be in a position that we should receive something. Absent such data, I think that we would be required under section 5 to basically sit there and say that, hey, we think we have a presumption here of: may present possible risk of widespread exposure, which is in the statute, and either hold up the granting of the study, or put it under tight requiremets by a Section 5(e) consent order or something like that. That would probably have the net effect of forcing them to go back and generate the data.

Mr. VOLKMER. You're going to be able to do that, to show that, without the data?

Dr. MOORE. We think we can do that much easier with a living microbe than we can with the chemical because of the statement in the statute that speaks to wide exposure. By the very nature of a living organism going out into the environment, I think that's a *priori* evidence that there is potential for wide exposure.[51]

The potential for widespread exposure to genetically-engineered organisms released into the environment should allow EPA to collect data on new organisms with more ease than has been observed in the "new chemical" program.

Drs. Riley and Mellon disagreed as to the implications of continued reliance on TSCA:

Mr. VOLKMER. But we still have a notification system rather than a permit system. Does that give you any concern?

Dr. RILEY. No, it doesn't give me concern, because if a dangerous organism were to be submitted in a premanufacturing notice to the RAC-like committee that would be formed to look at it, then I take it on faith that if there were danger involved, that RAC-like committee would impose certain requirements before that organism could be deployed to the environment.

So I can see that a PMN can actually function . . . with regulations. I can see that it could be made to work, yes.

Mr. VOLKMER. If sufficient information is provided in the pre-notification?

Dr. RILEY. Yes.

Mr. VOLKMER. There would have to be that?

Dr. RILEY. And that would have to be stipulated, yes, by the agency, what information is needed.

Mr. VOLKMER. Dr. Mellon?

Dr. MELLON. It does give me some pause. I am generally convinced that EPA is going to use the authority that it has under TSCA to vigorously regulate the products that come under its jurisdiction.

But it troubles me that if EPA should fall down on the job, an organism could be developed, notice given to EPA, no review conducted, and if EPA doesn't step in and do something about it, that organism will go on the inventory totally unreviewed and no one will have—that will be perfectly legal. No one will have any recourse; no one will be able to complain. You will be able to complain to EPA that it didn't do what you think it should have done, but you will not be able to go to court and charge it with failure to carry out a statutorily imposed duty.[52]

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[51] *Id.*, at 133.
[52] *Id.*, at 92.

Dr. Moore disagreed and provided a number of ways this would not happen.

Dr. MOORE . . . The procedures that EPA has established and which are explained in detail in the June 26 statements of policy ensure that reviews will be extremely thorough and scientifically credible. The procedure includes detailed review by EPA scientists with assistance from independent scientists, and peer review by the Biotechnology Science Advisory Committee.

Under TSCA once a microorganism is listed on the inventory of Existing Chemicals, other manufacturers can use it without submitting a new PMN. This is true for chemicals as well as microorganisms.

The fact that a microorganism is on the inventory means that it is not subject to PMN requirements, but it does not exempt it from other requirements of TSCA. In particular, sections 4, 6, 7, 8, and 13 of TSCA provide authority to regulate existing microorganisms under conditions that are specified in the statute. For example, section 6 allows the Administrator to regulate microorganisms if they may create a substantial hazard, and section 8 allows the Administrator to require reporting or record-keeping on existing microorganisms. Thus, these authorities provide EPA with legal recourse if there is reason to believe that a microorganism already listed on the inventory could cause harm to human health or the environment. In addition, concerned citizens may petition EPA under TSCA section 21 to take certain regulatory actions.[53]

2. FIFRA

EPA reviews microbial pesticides under FIFRA. Under this statute, the Agency may require an Experimental Use Permit before pesticides are used in the environment on more than ten acres of land. However, prior to publication of the Coordinated Framework, EPA operated under an interim policy that required notification to EPA before *any* field testing of genetically-altered or non-indigenous microbial pesticides for the purposes of determining the pesticidal qualities of the product.[54] If an application is of regional or national significance, or involves a new active ingredient or new use, EPA describes the experiment in the Federal Register for public comment.[55]

EPA announced in the Coordinated Framework that it will now implement two levels of review, depending on the nature of the microorganism.[56] This system reflects EPA's philosophy that the level of review should vary based upon the risks posed by the nature of the constructed microorganisms. Microbial pesticides not derived from pathogenic organisms would receive an "abbreviated" review. Most microbial pesticides are expected to be derived from pathogenic organisms and therefore receive the higher of the two levels of review.

The contrast between FIFRA's permitting scheme with TSCA's notification scheme prompted the following exchange:

Mr. VOLKMER. After reviewing . . . the problems with developing guidelines and regulations under TSCA, for any possible biotechnological chemical products, *should TSCA be change to a permitting scheme like FIFRA?*

Dr. MOORE. . . . In some respects, it would have some intuitive appeal. On the other hand, I think if you did it under TSCA, *you would be significantly changing TSCA from the way it was perceived, at least the agency perceives, as to what was intended when it was . . . enacted.*

. . . FIFRA . . . is a licensing statute and that is not the intent of TSCA. TSCA is a listing statute and a review mechanism. *So it would be a very significant change.*

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[53] *Id.*, at Appendix 5.
[54] 49 Fed. Reg. 40659.
[55] 51 Fed. Reg. 23323.
[56] *Id.*, at 23302.

I think that we do have a reasonable chance of being able to adequately control the biotechnology industry under the existing statutes of TSCA. As to whether or not one will be able to do it with the ease and facility that we all might like, I think it's probably best to answer when we get a little bit of experience. *We have yet, as we here, to receive the first thing under TSCA.*[57] [Emphasis added.]

D. USDA

USDA has both research and regulatory responsibilities for biotechnology activities. In July, 1985, the Secretary of Agriculture delegated responsibility to the Assistant Secretary for Marketing and Inspection (MI) for all matters pertaining to biotechnology regulation and to the Assistant Secretary for Science and Education (SE) responsibility for all matters pertaining to agricultural research involving biotechnology.[58]

With publication of the Coordinated Framework, USDA has set up a series of committees designed both to streamline the process for review and to allow input from both USDA divisions in the process.[59] The implementation of this new organizational structure was one focus of the hearing.

On July 14, 1986, the Secretary of Agriculture established the Office of Agricultural Biotechnology (OAB).[60] The OAB will implement and coordinate "the Department's policies and procedures pertaining to all facets of agricultural biotechnology.[61] It will receive "notices of all applications or requests received by the U.S. Department of Agriculture (USDA) for licenses, permits, or approvals of agricultural biotechnology products or research falling within the coverage of the *Federal Register* notice of June 26, 1986. . . . "[62]

While the OAB will provide administrative review and coordination of USDA's biotechnology program, the newly proposed "Committee on Biotechnology in Agriculture" (CBA)[63] will coordinate af-

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[57] "Hearing: Coordinated Framework", *supra,* note 14, Part I, at 132–133. In an earlier hearing, Mr. Steven Schatzow, then the Director, Office of Pesticide Programs was asked a similar question:

"Mr. VALENTINE. FIFRA requires that data be submitted to EPA before a permit is issued for the use of microbial pesticides. Under TSCA a company simply notifies the agency that it wants to market a project, for example, an organism that could be used in hazardous waste cleanup. Since EPA is charged with protecting the environment, doesn't it seem reasonable to have the same degree of prospective scientific review for organisms intended to be used in the environment under both FIFRA and TSCA?

"Mr. SCHATZOW. As I commented earlier, I think that is a real important question, and a very good one. I, having operated under the FIFRA statute for the last two years, can see some very strong benefits to having a licensing statute. I don't know that the agency would object to the conversion of TSCA into a licensing statute.

"What the agency would strongly object to, however, is carving out a certain subset of microorganisms and subjecting them, and only them, to this kind of licensing statute."

["H.R. 4452, the Biotechnology Science Coordination Act of 1986", joint hearings held before the Subcommittee on Natural Resources, Agriculture Research and Environment and the Subcommittee on Science, Research and Technology; June 4 and 5, 1986, (Hereinafter cited as "H.R. 4452.")]

[58] 50 Fed. Reg. at 29367–29368.

[59] *See* "Hearing: Coordinated Framework", *supra,* note 14, Part I, at Appendix 6; *See also* Appendix H, *infra.*

[60] Id., "Memorandum 1020–27", at 118.

[61] Id.

[62] Id., at 117.

[63] The CBA will be co-chaired by the Assistant Secretary for Marketing and Inspection Services, and the Assistant Secretary for Science and Education and will be comprised of policy-level representatives of the Agricultural Research Service (ARS), the Cooperative State Research Service (CSRS), the Animal and Plant Health Inspection Service (APHIS), the Food Safety and Inspection Service (FSIS), and the U.S. Forest Service (USFS).

fairs on a policy level, and will function as a "bridge between its research and regulatory structures".[64] USDA has also initiated the establishment of the Agriculture Biotechnology and Recombinant DNA Advisory Committee (ABRAC). This Committee will continue the responsibilities for agriculture formerly handled by the NIH/RAC during the last 10 years.[65] Applications for approval of research proposals submitted to the ABRAC are not published for comment, but certain portions of the ABRAC's meetings will be open to the public.[66]

Dr. Bentley explained that when applications are submitted to APHIS for a product license for a genetically-engineered organism, APHIS will notify OAB of the application concurrent with APHIS' review of the application. This will allow APHIS to process the application expeditiously, while still allowing others outside of APHIS the opportunity to provide APHIS with additional advice and expertise.[67]

In a letter to USDA, Mr. Volkmer questioned whether these new committees would in fact involve others outside of APHIS in the review of biotechnology products.

Mr. VOLKMER. Will any division or group outside APHIS review applications to license or move a genetically-engineered product?

USDA: The establishment of the Office of Agricultural Biotechnology (OAB) and the intra-Departmental Committee on Biotechnology in Agriculture (CBA) are administrative mechanisms to assist in determining those instances in which wider review of proposed releases would be appropriate and beneficial.

In general, divisions and/or groups outside APHIS review applications to license or move a genetically-engineered product . . .

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Additional review may be accomplished on an 'as needed' basis using mechanisms both within and outside of the Department consistent with Federal laws, rules, and regulations.[68]

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Mr. VOLKMER. Who will make the determination as to whether ABRAC reviews these proposed products or doesn't review them? Who makes that determination?

Dr. BENTLEY. Well, when you get to the final analysis on that, there is one point where we'd say the two assistant secretaries that are dealing with the CBA, that's why we have the CBA's . . . to look at questions like that where . . . there is some indecision as to whether it needed to go through the ABRAC. That's why I say there are . . . different levels of this. *Some cases it's clear, there's no question about it needs to go to the ABRAC. Sometimes it may not be, and the two assistant secretaries are at the policy level, if it needed to be approved.*

Now, most of the time I think . . . if one can draw on the experience of the NIH/RAC, many of the times that can be settled by the director of that office because there is a body of information and experience that's used as a protocol that would help us to go by that. So that's how we would generally approach it.[69] [Emphasis added.]

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[64] "Hearing: Coordinated Framework", *supra,* note 14, Part I, at 128.

[65] Id., at 115.

[66] Id., at Appendix 6.

[67] Further clarification of how applications to APHIS for genetically-engineered organisms would be handled was provided in an August 8, 1986 memo from APHIS to Dr. Bentley. "All notification to the OAB by APHIS will be made by the Biotechnology and Environmental Coordination Staff (BECS). The two APHIS agencies concerned with biotechnology, Veterinary Services (VS) and Plant Protection and Quarantine (PPQ), have developed . . . procedures . . . for reporting information to the BECS, which will in turn transmit the information to the OAB. In general, BECS will notify the OAB 5 working days after receiving a license or permit application, and 10 working days before final action on such an application."

[68] "Hearing: Coordinated Framework", *supra,* note 14, Part I, at Appendix 6.

[69] *Id.,* at 139.

Mr. Volkmer also wanted to know if the Science and Education division of USDA even had the regulatory authority to review license proposals for the release of genetically-engineered organisms. Dr. Mellon of the Environmental Law Institute stated that in her opinion it did not.

Dr. MELLON. . . . (Science and Education) is simply providing an opportunity out of the goodness of its heart for companies to have their . . . products reviewed. It doesn't have any authority for that review . . . I was wondering what would happen if USDA were to face an AGS-type situation where the guidelines laid down, or the procedures established, were violated.

I mean, what recourse would USDA have? EPA, acting under a very stringent and well-designed regulatory statute, could move and fine and use the power of the courts to make sure rules were adhered to. In the same situation, I don't think USDA would have any recourse other than persuasion.

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And perhaps just to shake its finger and say, "You shouldn't do that again." But it is not acting from any regulatory authority that I know of, in offering that review.[70]

Under the authority of the VSTA, USDA exercises regulatory authority over all veterinary biologics imported into the U.S. or shipped or delivered for shipment interstate, intrastate, or exported. Veterinary biological products must be prepared in a USDA-licensed establishment, and products imported into the United States must be imported under a permit.[71]

To clarify USDA's requirements for obtaining a VSTA license for genetically-engineered products, Mr. Volkmer asked whether USDA would accept from a license applicant supporting data (or test results) that the applicant obtained from another company when the other company obtained the data in a manner which did not comply with the NIH Guidelines or any other research guidelines. Ms. Darling replied, ". . . we cannot restrict research, or statutorily say this is how you have to run that test before you bring it to us".[72]

As this point has been a contentious one since the hearing on the licensing of the pseudorabies vaccine, Mr. Volkmer questioned Dr. Bentley further.

Mr. VOLKMER. Dr. Bentley, would that concern you, that . . . (the applicant) is) able to use (the data) . . . even though—that information . . . was illegally . . . (obtained)?

Dr. BENTLEY. Yes, it would.

Mr. VOLKMER. And you can't stop it, though?

Ms. DARLING. No.

Mr. VOLKMER. So that's something I think you better look at.[73]

Mr. Volkmer attempted to get further clarification on the involvement of the OAB and ABRAC in reviewing propoals for the release of genetically-engineered organisms under the VSTA.

Mr. VOLKMER. Now, . . . XYZ has submitted it to APHIS. When XYZ submitted that data and the application for the license, et cetera, all to APHIS, APHIS sent a notice over to OAB. Correct?

Ms. DARLING. Correct.

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[70] *Id.*, at 87–88.

[71] *See* VSTA, *supra,* note 85, Part II.

[72] "Hearing: Coordinated Framework", *supra,* note 4, Part I, at 137.

[73] *Id.*

Mr. VOLKMER. Now, OAB has got this notice and looking at it and saying, "Hey, that's just another . . . brucillosis vaccine or eradication serum; that's fine stuff. It doesn't look so bad to us." What will happen as far as the ABRAC is concerned? Will they get into it?

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Dr. BENTLEY. . . . It would seem to me that if that had been done without any type of approval, that the original company . . . would be in violation of the rule that says that organisms, if they use (genetically-engineered) organisms in this, should require—or would require approval at a national level.

Now, then . . . the question is, . . . this I can't answer for sure whether or not . . . such licenses as were requested can be granted. I don't know what the legal interpretation is of that, and I don't presume to speak to it.

But it would seem to me that that's the kind of question we have to face and will have to give attention to.[74]

Mr. Volkmer expressed his surprise that this situation had not yet been clarified within USDA.

Mr. VOLKMER. *The reason I brought that up is it's no different than what we talked about at our first hearings, Dr. Bentley.*

Still I don't think you've got them covered yet in your guidlines . . . [I]t's not covered in your rules, and it greatly concerns some of us that what we will see, releases into the environment out here, sometimes it may prove out that all that stuff is fine and it works fine just like it did in the pseudorabies vaccine. But lo and behold, the time will come when it isn't something that works out fine and we have a mess on our hands. That's what concerns me.

Dr. BENTLEY. Mr. Chairman, let me say one thing that I would like to pursue, and I am speaking now without knowing the restrictions of the law and various things because I am not familiar with all of the ramifications therein.

But it would seen to me that *this would be something we might want to consider in rulemaking at a future time,* and *that would have to be up to APHIS to adjudicate this,* whether or not—but it would at least be information on research.

Mr. VOLKMER. I think that any data that is going to be used in support of any license, there should be a requirement in the law, or else in the regulations if you don't want a law, at least in the regulations . . . (to certify that supporting) data has been obtained with approval . . . by USDA at least, similar to what EPA does——

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Mr. VOLKMER. Especially on genetically-engineered products that may be pathogenic or intergeneric types of products.

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Mr. VOLKMER. I think you need to look at that.[75] [Emphasis added.]

Similar questions were asked of USDA in a letter after the hearing. However, a different response was obtained at that time:

Mr. VOLKMER. Assume that you have two companies involved in developing a product eligible for licensing under the VSTA. The first company performs an unauthorized field test with the product. The second company then obtains the product from the first company and applies for a VSTA license based on the data from the unauthorized field test. Will USDA allow the second company to support the product based on data from the unauthorized field test?

USDA: *Data from an "unauthorized field test" performed by Company A cannot be used to support a USDA license application by Company B.*

An applicant for product license must demonstrate . . . all tests necessary to show that the product is safe, pure, potent, and efficacious. One of the initial steps in the licensing process is the preparation, characterization, and APHIS' acceptance of Master Seed stock (virus or bacterial culture).

Once the Master Seed is certified for use in a product, this material is used to prepare pre-licensing serials of vaccine as well as all vaccine that will be used to determine safety and efficacy data. Because this information must be developed by

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[74] *Id.*, at 137–138.
[75] *Id.*, at 138.

the license applicant, *the data from unauthorized field trials is essentially unusable in the APHIS licensing procedure.*

Mr. VOLKMER. Will a commercial institution applying to APHIS for a product license have to verify that all applicable research guidelines were followed in order to obtain a license?

USDA: In order to receive a veterinary product license, a firm must also have an establishment license issued by APHIS. USDA requires that commercial institutions applying for a product license verify that all applicable regulatory standards and guidelines be followed in product development. Licenses for the production of veterinary biological products are only issued under the Virus-Serum-Toxin Act (21 U.S.C. 151 et seq., 9 CFR Part 102).[76] [Emphasis added.]

Additionally, USDA continued, not only must all guidelines be followed, but, "APHIS will require IBC or equivalent review and approval of the research program prior to the initiation of any project employing recombinant DNA technology. IBCs certify that the proposed research program has been correctly categorized and that they are in compliance with the appropriate guidelines."[77]

With regard to the NIH Guidelines, the USDA Guidelines from the Proposed Coordinated Framework state that with respect to licensing for veterinary biological products derived from DNA technology, USDA *requires* all licensed applicants or products derived from DNA technology, to comply with the NIH Guidelines.[78] The new USDA Guidelines in the Coordinated Framework state that USDA *strongly recommends* that commercial applicants establish IBCs which follow applicable provisions of the NIH Guidelines.[79] In addition, it is clear from the Environmental Assessment performed for the licensing of the pseudorables vaccine that the data obtained from the unauthorized field test of almost 1,400 pigs with the vaccine was used to assure its potency, efficacy, purity, and safety for license approval.[80]

In addition to the VSTA, USDA has asserted jurisdiction over biotechnology products under the Federal Plant Pest Act (FPPA) and the Plant Quarantine Act (PQA). Under the FPPA, APHIS claims the authority to require a permit for the movement of any proven or suspected plant pest.[81]

At the hearing, Dr. Mellon expressed the opinion that:

. . . USDA apparently intends to assert enforceable authority over only one major category of organisms: plant pests, as defined under the Plant Pest Act.

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In USDA's opinion, organisms that are not plant pests simply do not need to be regulated. I quote from the policy statement: "Other genetically-engineered organisms which are engineered from certain organisms which are not plant pests are classified in taxa which do not contain plant pests need not be regulated." This is a remarkable statement. *Apparently, APHIS believes as a scientific matter that only those genetically-engineered organisms that are plant pests pose a threat to the environment. If so, APHIS's position is at odds with that of much of the scientific com-*

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[76] *Id.*, at Appendix 6.

[77] *Id.*

[78] 49 Fed. Reg. at 50900.

[79] 51 Fed. Reg., at 23340.

[80] *See* "Hearing: USDA Licensing", *supra*, note 13, Part I, at 199; and *See* discussion, *supra*, Part II, Chapter Three.

[81] Plant pest as defined by statute, means any living stage of any insects, mites, nematodes, slugs, snails, protozoa, or other invertebrate animals, bacteria, fungi, or parasitic plants or reproductive parts thereof, viruses, or any organisms similar to or allied with any of the foregoing, or any infectious substances, which can directly or indirectly injure or cause disease or damage in any plants or parts thereof, or any processed, manufactured, or other products of plants (7 U.S.C. 150aa[c]).

munity. It is also a position that is inconsistent with the USDA's ABRAC research policy, which describes lists upon lists of organisms that need regulatory oversight.[82] [Emphasis added.]

Dr. Mellon felt very strongly that reviews under the FPPA would be perfunctory at best, because their sole aim would be a determination of plant pest status. In the Coordinated Framework, USDA estimates that the cost of preparing a permit application will be no more than $5,000 per application and that no new data needs to be generated. The required information will include, among other things, descriptive data, country of origin, and quantities of planned introductions.[83] Dr. Mellon was clearly disturbed by the implications of this.

Dr. MELLON. While the notice claims that the information is supposed to be sufficient to allow USDA to assess the behavior of organisms in the environment, it will not be possible to do so with any degree of thoroughness with that kind of information. *None of the information on competitiveness or survival that is needed by other agencies, like the EPA, is asked for by USDA. It is scientifically impossible to understand how USDA could make an assessment of ecological hazard without ever requiring additional case-specific data.*

The APHIS review may allow the agency to make a determination of whether a plant is likely to be a plant pest, but in most cases, in my opinion, that determination would be a waste of $5,000. The objective of the regulatory review scheme is simply irrelevant to the mainstream scientific concerns about genetic engineering. Plant pests are part, but only a small part, of the problem. Restricting the movement of and inspecting and carefully packaging plants pests does not address the real problem.

Moreover, other than herbicides, it would not seem likely that many plant pests are going to be intentionally produced. *Of much greater concerns are organisms that are intended to do something beneficial and are therefore planned for release in large numbers into the environment. Under this approach, these organisms will not be reviewed or regulated at all.*[84] [Emphasis added.]

Another issue explored at the hearing, and in questions to USDA after the hearing, was whether a product had to be a proven plant pest before it could be regulated under the FPPA or the PQA, and whether USDA could require pre-release review of products of unknown plant pest status.

USDA: Under the provisions of the proposed USDA rule pursuant to the FPPA and PQA, *APHIS will require a permit prior to the introduction, which includes release into the environment, of a genetically engineered organism which is a plant pest or which USDA has reason to believe is a plant pest.* Proposed Section 340.0(a) prohibits any person from introducing a regulated article unless the introduction is authorized by a permit and such introduction is in conformance with all of the applicable restrictions contained in Part 340 (51 FR 23353, June 26, 1986).[85] [Emphasis added.]

Mr. Richard Godown of the Industrial Biotechnology Association agreed that the FPPA applied to genetically-engineered organisms:

. . . USDA's authority to prevent the introduction, spread, or establishment of plant pests appears to be broad enough to permit regulation of novel organisms created in a laboratory for release into the environment. Since the deliberate release of a genetically-engineered organism may result in the interstate movement of that organism, it is appropriate for USDA to treat such a deliberate release as if it is an interstate movement.[86] [Emphasis added.]

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[82] "Hearing: Coordinated Framework", *supra,* note 14, Part I, at 47; *See also* Appendix G, *infra.*

[83] 51 Fed. Reg., at 23360.

[84] "Hearing: Coordinated Framework", *supra,* note 14, Part I, at 48.

[85] *Id.,* at Appendix 6.

[86] *Id.,* at 156.

However, Mr. Godown did not agree that USDA could require a permit to regulate the movement of *suspected* plant pests:

. . . it seems plain that before USDA can require a permit or otherwise control the movement of an organism, it must first determine whether a suspected plant pest is in fact a plant pest. USDA's authority to make this determination is integral to its ability to regulate plant pests as required in the statute.[87]

While USDA is subject to NEPA, its limited authority under the FPPA reflects the fact that USDA's primary mandate is not the protection of the environment.

Dr. MELLON. The APHIS approach raises many questions about USDA's ability to protect broad environmental interests in the area of genetic engineering. As the USDA policy makes explicit, *USDA'S mandate is to protect and enhance agriculture and forestry in the United States. APHIS's narrow approach to the regulation of biotechnology is fully consistent with this view of its mandate, but an adequate response to the release of genetically-engineered organisms demands a concern for the total environment, not just of the agro-ecosystem.*

USDA's caution with regard to its mandate is justified. Congress has not charged USDA with protecting broad environmental interests. If it were to have stepped out boldly to protect the environment, it would have nothing to stand on except for the National Environmental Policy Act. And I think that would have proved to be a thin basis for a strong regulatory program.

This lack of mandate is the source of a gaping hole in the current biotechnology framework. EPA has such a mandate and is the better choice for the agency to regulate the broad environmental impacts of . . . the agricultural applications of biotechnology. But if Congress wants USDA to take on the task, new legislation mandating the protection of the environment as well as agricultural interests will be needed.[88] [Emphasis added.]

An additional difficulty in the review of proposals to release biotechnology products has been conflict within USDA over authority to review confidential business information (CBI). Up until now, APHIS officials have said that only APHIS personnel may review applications containing CBI, thereby depriving OAB and ABRAC of opportunities to review proposals. In response to follow-up questions about the handling of CBI, USDA replied:

Employees of the Federal Government, including special Government employees may not divulge confidential business information. Members, consultants, and advisors associated with both ABRAC and NBIAP, neither of which entities have existed in the past, will be "special Government employees." As such, they will be authorized to review confidential information after they have signed a commitment to protect such information . . .

The ABRAC will be provided with any information needed to discharge properly the responsibility assigned to it by the Department, which may include confidential business information. USDA will assure that ABRAC members act consistently with the provisions of the Trade Secrets Act (18 U.S.C. 1905).[89]

Dr. Mellon felt that the issue of CBI was both an important and difficult issue that needs to be resolved.

Dr. MELLON. I simply want to acknowledge that the . . . confidentiality of data is an extremely important and very difficult issue. I think companies have a legitimate proprietary interest in the information that they've developed as part of a product development.

At the same time, the public has a legitimate interest in the safety of the products that the companies are developing, and in the case of biotechnology it's extremely important that the public have an opportuntiy to see what . . . the products are and to judge what risks they present.

I have always been concerned that 5 years are going to elapse and that 20 organisms are going to have been reviewed and released into the environment that

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[87] *Id.*, but *see* Appendix G, *infra.*
[88] *Id.*, at 48.
[89] *Id.*, at Appendix 6.

nobody is going to know what they are, where they've been released, and what's happened after they've been released, because all that information is going to be held in an agency as confidential information.

If at the end, if that scenario is a correct one and the 5 years do elapse and an agency stands up and tells the public that the technology is safe, "Don't worry about a thing", I don't think that they're going to be believed. I think it's in the industry's interest as well as in the public's interest to try to resolve this; this conflict of interest here and arrange procedures by which members of the public can have access to the health and safety information that the companies develop.[90]

In addition to its policy statement on regulating commercial products, USDA published in the Coordinated Framework its proposed policy governing review of biotechnology research. USDA's research guidelines closely parallel the NIH Guidelines.[91] All phases of any USDA funded agricultural research or research conducted at an entity receiving USDA funds are subject to the Guidelines unless it is subject to another agencies' guidelines or regulations. It is clear from the USDA Guidelines that the Agencies' intention is that local Institutional Biosafety Committees (IBCs), patterned after those mandated in the NIH Guidelines are to play an important role in monitoring different phases of biotechnology research.[92]

Two questions posed by Mr. Volkmer both during and after the hearing asked the witnesses if IBCs, as presently devised, are capable of adequately carrying out the responsibilities assigned to them in the USDA Guidelines.

Dr. MELLON. *Probably not.*

IBCs vary tremendously in their make-up, dedication and performance. *It is hard to generalize about them, but it seems unlikely that local committees, however constituted, are the proper vehicle for implementing policy in an area as scientifically underdeveloped as this one.* To begin with, IBCs cannot be counted on to have the requisite ecological expertise to answer, or even to ask, questions about ecological impacts. Furthermore, it seems unlikely that scientific reviews done by scattered local committees could ever generate the kind of information that would be useful in resolving the questions about scientific risk.[93] [Emphasis added.]

Mr. Volkmer asked if IBCs would be capable of certifying research proposals for compliance with the policies of different Federal Agencies. Dr. Riley replied, "I have wondered whether there might be a way for the IBCs to perform a constructive role at the campus level, but I am aware that there . . . have been no decisions along those lines yet. . . . But I also can see that the individual IBCs cannot take any kind of definitive action in this arena at the present time.[94]

A number of other questions about the proposed functioning of IBCs were clarified by USDA in a letter to the Subcommittee:

Overall responsibility (for IBCs) will continue to rest with NIH. In agricultural matters, however, the OAB will monitor the composition and decisions of each IBC for compliance with the USDA Guidelines. In addition, ABRAC will have the re-

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[90] *Id.*, at 91.

[91] USDA issued the Guidelines under the authority of the Food Security Act of 1985 (Public Law 99-198) which gave the Secretary of Agriculture responsibility for establishing "appropriate controls with respect to the development and use of the application of biotechnology to agriculture." *See* 51 Fed. Reg. at 23367-23393.

[92] *Id.*, at 23390.

[93] "Hearing: Coordinated Framework", *supra*, note 14, Part I, at Appendix 3.

[94] *Id.*, at 87.

sponsibility under the USDA Guidelines to assure the IBC's agriculture-related capability and will cooperate with NBIAP at the local level.

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Although it is not explicit in the advanced notice, it is intended that if researchers disagree with an IBC decision, they are free, as in the NIH/IBC system, to appeal to the national level. In that case, AB would then determine whether to concur with the IBC, reverse the IBC, or refer the question to ABRAC.

The IBC's were included as an element of the NIH/RAC procedure. The USDA proposes to use these same committees to avoid duplication of effort. The membership of specific IBCs may need some supplementation to assure capability to evaluate agriculture/related proposals and to comply with the membership requirement in the proposed USDA Guidelines (Section 403, 51 FR 23389) . . .[95]

E. General Comments

At the hearing, Congressman Scheuer, criticized the Coordinated Framework for leaving "open and unresolved", many questions that should have been addressed.[96] He cited as examples delays inherent in the rulemaking process, the fact that critical definitions were lacking—such as "release into the environment,"—and the confusing explanation of Charts I and II provided in the preamble. Mr. Scheuer also felt that businessmen trying to interpret the guidelines would find themsleves utterly confused as to where to go for advice and counsel in matters regarding their products.

Mr. Packard did not agree that the guidelines were confusing to scientists:

Mr. Packard. I think that to the novice and to the uninformed and those that are not involved in this process, regulations are always complex, and certainly these would be complex to the nonscientist and to the nonresearcher. But to the researchers, I think they have been crying for guidelines and they would rather have guidelines that their scientists can get into, and they will understand them, in my judgment, even though you and I may not, because of our backgrounds.[97]

There were other criticisms of the guidelines voiced both at the hearing and in responses to questions posed of the witnesses after the hearing.

Dr. Mellon. . . . It disturbs me that the biotechnology policy pays very little attention to what appears to many to be the central feature of the deliberate-release issue: its scientific uncertainty. Scientists have not yet determined whether or not the release of engineered organisms represents a serious economic and environmental threat. In the absence of data, plausible scientific cases can be made to support both positions. This is the soft sort of underbelly of the entire deliberate-release issue. If the Federal Government chooses to control the technology at this early stage before its risks are understood, it must also attempt to resolve the uncertainty about the nature of those risks.[98]

Another criticism centered on the fact that the provisions for collection of data on genetically-engineered organisms provided in the guidelines may not be adequate.

Dr. Mellon. . . . the guidelines contain no mechanism to systematically compile the information that will be collected by agencies so that it can be used in determining what are the actual risks associated with the releases of engineered organisms.[99]

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[95] *Id.*, at Appendix 6.
[96] *Id.*, at 36.
[97] *Id.*, at 38–39.
[98] *Id.*, at 48–49.
[99] *Id.*, at Appendix 3.

Dr. Norse agreed with Dr. Mellon.

Dr. NORSE. . . . we find ourselves in the middle between the uninhibited enthuiasm of the industry and the unyielding opposition of some nonscientists. But we also find that the scientists who have so far dominated the discussion of biotechnology don't understand the interactions of living things in their environments well enough to justify their assertions that the risks are insignificant. Consequently, our enthusiasm about genetic engineering is tempered with caution.

The coordinated framework seeks to do something very difficult: to create consistency in regulating diverse engineered orgaisms by diverse agencies. Unfortunately, I believe that the preamble is questionable in both science and policy because it leans too far toward allowing releases without appropriate safeguards.[100]

On this subject, Dr. Riley felt the provisions, ". . . could be made to work, whether the avenue is a premanufacturing notice or an application for a use permit." However, she added that, "Whether these mechanisms will in fact be adequate in practice depends on how the guidelines are interpreted and implemented in the form of specific information requirements and review practices." [101]

Dr. Riley also suggested that, ". . . more detail concerning the characteristics of the target environment be sought from the investigator at early stages of information gathering. It is the relationship between a genetically altered organism and a designated environment that determines the element of risk or safety of a combination of the two. Therefore, a description of the intended environment is of primary importance." [102]

F. SUMMARY

The Coordinated Framework breaks new ground, both in the United States and abroad, in the regulation of biotechnology. It represents a comprehensive effort to forge a cautious but flexible system to review the environmental release of genetically-engineered organisms.

The Coordinated Framework relies for its success on consistent implementation by the various agencies of existing statutes that are expected to address the different levels of risk as defined by the BSCC. The following chapters discuss those definitions, the delegation of jurisdiction among the agencies and the authorities upon which the agencies will rely.

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[100] *Id.*, at 73–74.
[101] *Id.*, at Appendix 2.
[102] *Id.*, at 60.

CHAPTER TWO: DEFINITIONS

The controversy which surrounds biotechnology is due in large part to the absence of precise definitions for key terms, including the term "biotechnology" itself. This ambiguity has interfered with the implementation of biotechnology regulations.

The Federal policy for the regulation of biotechnology has been primarily directed towards "genetically-engineered organisms." The term "genetically-engineered" is itself a catch-all phrase; some use it to refer to an organism derived through recombinant DNA technology, while others use it in a broader context. Dr. Edward Adelberg reviewed this conflict at a 1985 conference on "Engineered Organisms in the Environment".[103]

> "Genetic engineering" refers to all methods by which mankind has manipulated the genomes of plants, animals, and microorganisms for practical ends—including controlled breeding with artificial selection, mutagenesis, gene transfer, nuclear transplantation, and embryo fusion, as well as recombinant DNA techniques. Whether we are introducing an "old" (that is, naturally occurring) organism into a new environment or a "new" (that is, genetically-engineered) organism into an old environment, the concern is the same: will the ecosystem be affected in a harmful or undesirable way? [104]

The Proposed Coordinated Framework states that recombinant DNA techniques involve the "*joining pieces* of DNA from different organisms or synthetic DNA together *in vitro*".[105] This definition is incomplete in a practical sense, since scientists comprising the NIH/RAC have not limited their oversight to organisms which have been altered through the addition of genetic material. Since 1982, the RAC and EPA have spent considerable time reviewing a proposal to field test ice-minus, an organism that was altered through the deletion of a gene.[106]

This conflict in defining "recombinant DNA techniques" was highlighted at the hearing which investigated USDA's licensing of the genetically-altered pseudorabies virus vaccine.[107] At that hearing, Dr. Kit maintained that the recombinant DNA guidelines were not applicable in the case of the pseudorabies virus because the organism was altered through the deletion, rather than the addition, of genetic material. Dr. Kit told the Members that, while it was true that a live virus vaccine had been used to immunize almost 1,400 swine on a West Central Texas farm, this did not conflict

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[103] "Engineered Organisms in the Environment", June 10–13, 1985, proceedings available from American Society for Microbiology, Washington, D.C. *See* also A.H. Teich, M.A. Levin, and J.H. Pace (eds.), *Biotechnology and the Environment: Risk and Regulation*; (Washington: American Association for the Advancement of Science, 1985).

[104] H.O. Halvorson, D. Pramer, and M. Rogul (eds), *Engineered Organisms in the Environment: Scientific Issues.* (Washington: American Society for Microbiology, 1985). (Hereinafter cited as "Engineered Organisms in the Environment"), at 233.

[105] 49 Fed. Reg., at 50907.

[106] *See* discussion, *supra,* at Part II, Chapter Two.

[107] *See* discussion, *supra,* at Part II, Chapter Three.

with the prohibitions on such research since the organism in question did not contain recombinant DNA.

Mr. VOLKMER. It is not . . . a recombinant product?

Dr. KIT. No, sir. *This particular product does not have any DNA from two species mixed together.* And, secondly, it was not constructed in the test tube, which is the definition that I have seen for recombinant DNA. This material is made by a normal process which occurs in all cells all of the time, . . .

Mr. VOLKMER. . . . you don't replace any gene, but you do remove a gene?

Dr. KIT. That's correct.

Mr. VOLKMER. And what you are saying is, when you remove a gene and not replace it with anything else, it is not recombinant DNA?

Dr. KIT. No, no; I haven't said that at all.

I said the recombinant DNA, sir, is defined a very specific way in the guidelines and is defined actually, historically in the original experiment by Berg, Symons & Jackson, which was fusing together a Lambda DNA in the test tube with a Simion [sic] virus 40 DNA. It was mixing of two taxonomic species in the test tube to provide an organism that could replicate both in bacteria and in animal cells. Our virus has nothing to do with this . . .

Mr. VOLKMER. . . . your position, is that this does not fall into the guidelines because basically it is not recombinant DNA procedures that are used to produce a product.

Is that correct? In layman's language?

Dr. KIT. I am attempting to emphasize very clearly, my laboratory, since 1979, has been engaged in recombinant DNA technology as understood in the guidelines. That is, in the use of plasmids containing foreign inserts of animal genes, the thymidine kinase gene, and other such techniques. And that all of these techniques are important and contribute to amassing the information which makes possible the scientific experiment of marker transfer to give not by splicing, but by normal events in the cell—a deletion mutant that we seek . . .

Mr. VOLKMER. Yes, but not to enhance the deletion of the TK, did not you produce the deletion in the laboratory?

Dr. KIT. We set up the conditions for the deletion to occur by providing millions of tissue culture cells with infectious DNA and the fragment of DNA which contained a thymidine kinase gene suitably altered . . . there is a finite possibility that some exchange of DNA fragments will occur in a cell during the mating process and during the normal replication process of the virus in the cell . . .

This is not the definition of recombinant DNA technology in the Federal Guidelines—excuse me, of a recombinant DNA molecule.[108]

Notwithstanding Dr. Kit's analysis, the NIH/RAC has consistently concerned itself with deletions produced through recombinant DNA techniques.[109]

The deletions were produced by recombinant DNA techniques and were thus considered a legitimate concern of the RAC, even though spontaneous or induced mutants of identical or similar phenotype are known and are, of course, entirely outside the RAC's concern.[110]

The Coordinated Framework defines the level of review different types of genetically-engineered organisms will receive.[111] The type of genetic material used to construct an organism determines whether it will receive full or abbreviated review before it is used in an uncontained setting.

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[108] "Hearing: USDA Licensing", *supra,* note 13, Part I at 170–172.

[109] On September 29, 1986, the NIH/RAC approved an amendment to the definition of deliberate release in Section IIIA–2 of the NIH Guidelines. Organisms in which the only use of recombinant DNA has been to remove or rearrange genetic information within a genome would be exempt from RAC review and NIH and IBC approval prior to release into the environment. This exemption, which has been in effect for laboratory experiments, is now being applied to environmental release experiments. The Director of NIH must approve the amendment before it goes into effect.

[110] "Engineered Organisms in the Environment", *supra,* note 104, Part III, at 233.

[111] 51 Fed. Reg. 23307.

Specifically, the Coordinated Framework proposes that pathogens and organisms altered to contain genetic material from another taxonomic genus be subject to full scientific review prior to their use in the environment. The BSCC excludes from the definition of "pathogens", organisms such as competitors or colonizers of the same substrates, commensal, or mutualistic microorganisms, or opportunistic pathogens. This exclusion implies that not all potentially pathogenic organisms will receive full scientific review. Opportunistic pathogens are organisms that can cause disease in animals, plants, or humans, whose natural resistance has been reduced either through wounds which permit the organism to gain access or through underlying conditions which compromise the immune response.[112] Organisms are generally viewed as opportunists in relation to a specific host or environment. The exclusion of opportunistic pathogen from the definition of pathogen excludes them from the higher level of review given pathogens. This raises concerns because it may not be known in advance whether an opportunistic pathogen will in fact be virulent in a particular environment.

Similarly, organisms containing alterations which do not involve genetic material from a different taxonomic genus or which contain alterations in non-coding regulatory sequences would be subject only to an abbreviated form of review prior to their use in the environment. The abbreviated review of certain types of genetically-altered organisms was discussed by scientists at the hearing on the Coordinated Framework. Dr. Monica Riley said:

First, we do not favor exemption of intergeneric hybrids that contain only regulatory sequences in the introduced DNA.

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. . . we believe that there should be no distinction made between the level of review afforded to noncoding and to coding sequences. The reason for this is: Although in most cases . . . a foreign regulatory sequence will be entirely innocuous, still one must take into account the fact that some regulatory sequences have the capability to increase the expression of the associated gene very many-fold. Also, regulatory sequences carry specificity determinants which govern when a gene is turned "on" and "off" in response to chemically specific signals.

Although it is true that regulatory sequences do not affect the composition of the gene product in any way, there is the possibility of major quantitative changes in the amount of gene product produced and changes in the signal which would turn the gene "on" that could possibly in some cases cause problems.[113] [Emphasis added.]

Dr. Elliot Norse of the Ecological Society of America added:

Altering regulatory sequences and deleting genes can affect an organisms' survival, reproduction, and have environmental effects. I surmise that the rationale for exempting these alterations is that if no sequences coding for proteins are modified, changes will be merely quantitative and, hence, minor.

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Regulatory sequences that change growth and reproductive rates by just a few percent could dramatically alter competitive balances among organisms in nature.[114] [Emphasis added.]

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[112] R.Y. Stanier, E.A. Adelberg, and J. Ingram, *The Microbial World,* Fourth Edition, Prentice-Hall, Inc., Englewood Cliffs, N.J.

[113] "Hearing: Coordinated Framework", *supra,* note 14, Part I, at 60.

[114] *Id.,* at 75.

Dr. Riley explained that in most cases, changes in regulatory sequences will have no substantive effect on the organism's interaction with its environment, while in other cases an organism may in fact be greatly altered. She added that the most critical feature to consider in deciding whether or not to release an organism into the environment is not what has been done to alter the genetic composition of the organism but how the organism relates to the environment.

It is the relationship between a genetically altered organism and a designated environment that determines the element of risk or safety of a combination of the two. Therefore, a description of the intended environment is of primary importance.

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. . . all pathogens and their derivatives, no matter what the alteration, *should be scrutinized before being introduced into the environment.*[115]

Another area of confusion is the definition of what constitutes the release of a genetically-engineered organism into the environment. Since the inception of the NIH Guidelines, a general understanding of this term has been that release occurs if an experiment does not take place within the confines of a laboratory where the organism can be physically contained and remedial measures taken in the event of an accident.[116]

At the hearing on the ice-minus organism, Dr. Bedbrook told the Members that AGS scientists concluded that injecting live, genetically-engineered organisms into the woody tissue of a tree did not constitute the release of these organisms into the environment. The fact that for several days sap leaked from the site on the tree at which several million bacteria had been injected raises some question as to whether the organisms were truly contained within the tissue of the tree.[117]

Similarly, Dr. Kit maintained that inoculation of a swine herd was not a "release." However, part of the study focussed on whether the animals shed the genetically-engineered live virus and thereby "released" it.[118]

The conflict over the term "release into the environment" was further highlighted by representatives of the American Society for Microbiology.

Dr. SCHAECHTER. There are types of releases and types of releases. If one was to take a county full of strawberries and release organisms overnight, that's quite a different dimension and quite a different concern than if one was, in fact, inoculating animals in a confined environment.

Mr. VOLKMER. In a confined environment, but not to say whether you're inoculating 1400 animals in a nonconfined environment?

Dr. SCHAECHTER. That's quite different.

Dr. RILEY. As far as inoculating animals with a live virus that—I believe the physiology and biology differs one example to another and that there are some physiological situations where the inoculated animals will be putting out live virus just as they were given it, either, you know, from a runny nose or whatever, but in other types of physiological situations the place where the virus goes is really sequestered; it may be along nerve shafts, and so forth, and they do not come out again, so—in my way of thinking there might be the possibility of inoculation with a vaccine to

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[115] "Hearing: Coordinated Framework", *supra,* note 14, Part I, at 60.

[116] "Hearings: H.R. 4452", *supra,* note 57, Part III. As Dr. Moselio Schaecter, President of the American Society for Microbiology said, "If you can't sterilize it, there is a risk that (it) can spread in the environment."

[117] *See* discussion, *supra,* at Part II, Chapter Two.

[118] *See* discussion, *supra,* at Part II, Chapter Three.

animals where it really constitutes virtually no risk because of the physiology. So I think that has to be examined and that's part of the risk assessment chore—is to look case by case and to decide whether this is one that proliferates and spreads or this is one that just goes to ground as soon as you've inoculated the animal.[119]

The confusion regarding the terms "containment facility" and "release into the environment" was not resolved in the Coordinated Framework:

While the concept of physical containment may imply the high containment conditions found in certain laboratories and greenhouses, in agricultural practice many simpler effective barriers are routinely used; these include microplots for soil bacteria and fungi, paddocks for noninffective animals, and removing or covering the reproductive parts of plants and animals.

"Release into the environment" for the time being, will have somewhat varying definitions for the regulatory and research review of the different agencies. There may be minor differences between agricultural and nonagricultural approaches and between macro- and microorganisms.[120] [Emphasis added.]

OSTP has asked for public comment on an appropriate definition of the term "release into the environment" [121] and has formed a subcommittee to develop guidelines for containment facilities such as greenhouses. The final definition is expected to be available in early 1987.[122]

A. Summary

The BSCC has admittedly not completed its work of finalizing definitions that are crucial to full implementation of the Coordinated Framework. The ice-minus case and the testing of the pseudorabies vaccine in West Texas demonstrate the confusion still surrounding the concepts of "release into the environment" and "contained facility".

The definitions contained in the Coordinated Framework will have significant regulatory impact by determining how different classes of organisms will be reviewed prior to their use in the environment. The use of abbreviated review for organisms containing alterations in non-coding regulatory sequences and opportunistic pathogens raised several concerns. The risks these organisms may pose should not be decided solely on the basis of their genetic alteration but should be determined by analyzing the interactions of the organisms in specific environments as well.

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[119] "Hearings: H.R. 4452", *supra,* note 57, Part III.
[120] 51 Fed. Reg., at 23307.
[121] *Id.*
[122] *See* "Hearing: Coordinated Framework", *supra,* note 14, Part I, at 10.

CHAPTER THREE: JURISDICTION

The establishment of clear regulatory jurisdiction among and within the federal agencies is a major goal of the Coordinated Framework. The following section discusses how the Coordinated Framework addresses the question of product and research jurisdiction.

A. Jurisdiction To Regulate Commercial and Research Products

Under the Coordinated Framework, Jurisdiction to regulate the manufacture and release of biotechnology products is determined by a product's use. Thus, FDA reviews foods, food additives, human drugs, medical devices & biologics and animal drugs. USDA reviews animal biologics,[123] plants, animals, microorganisms with agricultural uses, and potential plant pests. EPA reviews pesticides, microorganisms in contained uses, and microorganisms used for non-agricultural purposes.[124]

This scheme allows for considerable overlap of jurisdiction between EPA and USDA. Anything that EPA reviews that could also be a plant pest, an animal pathogen or a "regulated article," USDA reviews as well.[125]

Although EPA and USDA have entered into Memoranda of Understanding and have stated that they will work cooperatively and simultaneously to evaluate genetically-engineered organisms and products falling under dual jurisdiction, questions remain regarding the way in which review of a product by the two agencies will occur. Timeliness and depth of review may pose a problem in some situations.

For example, "intergeneric" organisms [126] may be regulated by both APHIS and EPA.[127] EPA may require only a pre-manufacturing notification, while USDA may require a permit for a field test. Without adequate cooperation between the agencies, the product approval process could be time-consuming and confusing.

Biotechnology research jurisdiction under the Coordinated Framework is based on a "lead agency" system. If more than one agency has potential jurisdiction, one agency is designated as a

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[123] 51 Fed. Reg. at 23311.
[124] *Id.*, at 23304.
[125] *Id.*
[126] *Id.*, at 23307.
[127] "Intrageneric" organisms are those that aren't intergeneric. If the source organism is pathogenic, and the microorganism is used for agricultural purposes, APHIS has jurisdiction. If it is used for non-agricultural purposes, EPA has jurisdiction; APHIS could be involved if it is a "regulated article" requiring a permit. If the intrageneric organism contains no genetic material from a pathogen, EPA has jurisdiction, requiring only an informational report. "Non-engineered pathogens" used in agriculture fall under APHIS jurisdiction while those for non-agricultural uses come under EPA with APHIS involvement if the microorganism is a regulated article requiring a permit. Non-engineered, non-pathogenic microorganisms are under EPA jurisdiction requiring only an informational report.

lead agency. That designation depends on who is funding the research, or which regulatory agency reviews specific purpose research (e.g. pesticides).[128] When the lead agency is the funding agency, the review and approval of research protocols will be conducted by NIH, NSF, or USDA's Science and Education Division.[129]

Dr. Kingsbury explained the "funding agency" concept as follows:

> If you have Federal funding, you are responsible to the agency which funds your research . . . I think it's very clear, and that's unequivocal. If you have an NIH grant, then you deal with the NIH. I think that that is very clear for anybody, and I think the scientific community is very accustomed to that notion.[130]

Dr. Kingsbury stated in a response to a letter from the Subcommittee that,

> Each funding agency is working from a standard set of guidelines and making individual determinations which review committee should be contacted to examine a specific proposal. Once that committee has been provided with the necessary materials it will be in direct contact with the investigator to obtain any additional information that may be necessary. This is a very simple and direct mechanism with a minimum of bureaucratic intervention.[131]

This system appears rife with conflict. Two and sometimes three agencies or divisions could review a proposed release. Calling for the funding agency to review proposed releases (except in the case of microbial pesticides) could lead to similar organisms being reviewed in dissimilar ways—something the Coordinated Framework was specifically designed to avoid.

For example, USDA has funded 87 research proposals that could lead to environmental release within the next five years.[132] When USDA was asked if copies of the proposals had been made available to other federal agencies who might have jurisdiction over the various products, USDA stated:

> When the proposals are received and our final procedures are implemented, project information will be provided to agencies which might be involved with product release for commercialization.[133] [Emphasis added.]

This implies that other agencies will be provided with relevant information only if the release is to lead to product commercialization.

Conflicting jurisdiction within USDA has also been a major problem. Oversight in the area of biotechnology research falls to the Assistant Secretary of Science and Education while review of commercial applications is under the Assistant Secretary for Marketing and Inspection. Marketing and Inspection has general regulatory authority and expertise, but most of the special biotechnology

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[128] According to the Coordinated Framework, research on plants, animals and animal biologics could require an APHIS permit if a "regulated article", plant pest or animal pathogen is involved. EPA has authority for all environmental research on microbial pesticides regardless if the project receives federal funding or not.

[129] The new USDA Guidelines, patterned after the NIH Guidelines apply to agricultural research on plants, animals and microorganisms. If an institution receives financial support from NIH, Science and Education or NSF, adherence to the appropriate set of guidelines is required. Some experiments require individual approval by the respective agency providing institutional support.

[130] "Hearing: Coordinated Framework", *supra,* note 14, Part I, at 38.

[131] *Id.,* at Appendix 1.

[132] *See* "USDA Biotechnology Research," *supra,* note 1, Part I.

[133] "Hearing: Coordinated Framework", *supra* note 14, Part I, at Appendix 6.

expertise exists within Science and Education. In the past, this split of authority and expertise has caused confusion in the biotechnology industry regarding who within USDA should review proposals to field test biotechnology products.[134]

Although USDA formed the Agricultural Recombinant DNA Research Committee (ARRC) in 1976 to oversee policy matters on recombinant DNA research and to coordinate research policies among the various agencies in USDA (and between USDA, NIH, and NSF) it has never truly functioned as the focal point of USDA's review of biotechnology.[135] Recent hearings before the Investigations and Oversight Subcommittee showed that no mechanism exists under USDA's present statutes that would even enable the ARRC to participate in the review of the application for product licenses.[136]

The confusion about responsibility for biotechnology review in USDA is not solved by the Coordinated Framework. For example, the Coordinated Framework gives APHIS primary responsibility to review research-oriented releases for USDA. This contradicts USDA's announced policy of giving the Science and Education division jurisdiction to review research programs.

B. Summary

Several factors hinder the establishment of clear regulatory jurisdiction under the Coordinated Framework. First, the statutes relied upon by the agencies give different agencies jurisdiction at different times in a products development. For example, EPA has jurisdiction over pesticides and the commercial manufacture of "new" organisms. If it later becomes known that the pesticide is also a plant pest or that the "new" organism has agricultural uses, USDA has jurisdiction. USDA has jurisdiction over research it funds, but if the research produces a pesticide, both USDA and EPA would have regulatory jurisdiction. Second, in addition to being overlapping, the jurisdiction may be significantly different—USDA may have permit authority, while EPA can only require a data report. Such a difference complicates the cooperation by the two agencies. Finally, USDA has not clearly established how it will divide jurisdiction between its major divisions to use both to their best advantage.

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[134] *See* discussion, *infra, Appendix A.*
[135] *See* "USDA Biotechnology Research," *supra,* note 1, Part I.
[136] *See* discussion, *supra,* Part II, Chapter Three.

CHAPTER FOUR: AUTHORITY

A. General Principles

Since the advent of genetic engineering, Congress has passed no laws specifically designed for the regulation of biotechnology products released into the environment. The Administration's policy, as expressed in the Coordinated Framework, is that "existing statutes provide a basic network of agency jurisdiction over both research and products; this network forms the basis of this coordinated framework and helps assure reasonable safeguards for the public."[137] This view was reinforced by the conclusions of the interagency working group of the White House Cabinet Council on Natural Resources and Environment in the Spring of 1984. That working group determined that, for the most part, existing laws as currently implemented would adequately address the regulatory needs of biotechnology, and that additional regulatory requirements could be implemented under existing statutory authority.[138]

Underlying the reliance on existing authority is the belief that utilization of existing health and safety laws could provide more immediate regulatory protection and certainty in the biotechnology industry and would avoid the "vagaries of untried approaches."[139]

In addition, there is the concern that the broad spectrum of biotechnology products preclude the development of any alternative unitary statutory approach intended to regulate biotechnology products as a whole.

The preamble to the Coordinated Framework recognizes the difficulties in a system that relies on existing law—i.e., inconsistent terminology and uneven standards of review in the various agencies:

> Because this comprehensive regulatory framework uses a mosaic of existing federal law, *some of the statutory nomenclature for certain actions may seem inconsistent.* Certain laws, such as USDA's Federal Plant Pest Act, require a "permit" before a microorganism pathogenic to plants may be transported or imported. Under other laws such as FIFRA, the agency "licenses" or "approves" the use of a particular product. TSCA requires a "premanufacturing notification (PMN)". There are also some variations among the agencies in the use of the phrase "genetic engineering". Regardless of the nomenclature, the public should be aware that the reviews conducted by each of the regulatory agencies are intended to be of comparable rigor. Agencies have agreed to have scientists from each other's staff participate in reviews. Each regulatory review will require that the safety, or safety and efficacy, of a particular agricultural or industrial product be satisfactorily demonstrated to the regulatory agency prior to commercialization.[140] [Emphasis added.]

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[137] 51 Fed. Reg., at 23302.

[138] *Id.*

[139] Korwek and Cruz, *Federal Regulation of Environmental Releases of Genetically Manipulated Microorganisms,* Volume II, Rutgers Computer and Technology Law Journal 303 (1985) at 382.

[140] 51 Fed. Reg., at 23303.

The following section examines how EPA and USDA propose to use their respective statutory authority to implement the Coordinated Framework.

B. EPA

EPA proposes to regulate genetically-engineered microorganisms under two statutes, TSCA and FIFRA.

1. TSCA.—Under TSCA, EPA will require pre-manufacturing notification prior to the environmental release of intergeneric organisms or pathogenic organisms and will require production and exposure data for all other types of genetically-engineered organisms. EPA plans to promulgate rules to subject research and development activities and small businesses to TSCA's notification and reporting requirements. As Dr. Moore of EPA noted, TSCA requires "notification" and reporting because it is a "listing" statute, not a licensing one.[141]

EPA's plan to regulate genetically-engineered microorganisms under TSCA raises several concerns. The most common criticism is that EPA has consistently failed to obtain sufficient data on new chemicals regulated by TSCA.[142] EPA responds to such criticism by noting that it often negotiates voluntary agreements with the manufacturer to provide additional data to reassure EPA reviewers of any possible risk concerns. EPA officials also note that, because risk is a function of hazard and exposure, EPA often cannot justify requests for hazard data on chemicals if exposure is estimated to be low. However, because genetically-engineered organisms can reproduce, and there is the potential for widespread exposure, EPA expects to be able to gather more data on biotechnology products than on chemicals.[143]

Another difficulty in applying TSCA to biotechnology products is the "listing" nature of TSCA. There is a presumption under TSCA that a product is safe unless EPA can show otherwise. This presumption may not be appropriate in regard to biotechnology products especially "intergeneric" or pathogenic organisms, until more research is done on the environmental effects of releasing various types of genetically-engineered organisms.

TSCA may be deficient for biotechnology regulation in that it presently exempts reseach and development activities in general, and activities of small businesses in particular from most of its provisions. Although EPA intends to promulgate rules to make TSCA more suited to biotechnology, the process will take several years during which time EPA must rely on voluntary compliance.

Although there have been no reviews under TSCA as yet, TSCA's reliance on rules for regulating individual substances could prove unwieldy for biotechnology products once applications are submitted. The diversity of genetically-engineered microorganisms may defy any effort by EPA to promulgate regulatory rules on a case by case basis.

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[141] *See* discussion, *supra,* Part III, Chapter One.

[142] *See, Assessment of New Chemical Regulation Under TSCA*—GAO/RCED 84-84, June 15, 1984.

[143] *See.* "Hearing: Coordinated Framework", *supra,* note 14, Part I at 133.

2. FIFRA.—EPA has long used FIFRA to regulate microbial pesticides.[144] Under its interim policy, EPA required notification at least 90 days prior to any small scale field testing of non-native and genetically-engineered microorganisms used as pesticides.[145] If EPA identified problems with the use of the microbial pesticide, it could require the company to submit the considerable data required to obtain an Experimental Use Permit.[146]

EPA has used FIFRA to regulate ice-minus as well as Monsanto's microbial pesticide containing *Bacillus thuringiensis*.[147] Implementation has been troublesome because data requirements and review procedures for genetically-engineered organisms have not been well-defined.

C. USDA

USDA bases its authority to regulate biotechnology products under several statutes; these primarily include the Virus-Serum-Toxin Act,[148] the Federal Plant Pest Act,[149] the Plant Quarantine Act,[150] The Organic Act,[151] and the Noxious Weed Act.[152] In addition, USDA relies on two Memoranda of Understanding to provide guidance concerning jurisdiction issues between USDA and EPA and USDA and FDA.[153]

(1) The Virus-Serum-Toxin Act (VSTA) was originally enacted in 1913 to license the interstate sale or shipment of veterinary biologics. It was amended in 1985 to cover intrastate sales or shipments. Other than shipment, the VSTA does not regulate academic research for genetically-engineered organisms outside of licensed establishments or prior to the filing of a license application. This limits its ability to regulate the release of genetically-engineered veterinary biologicals.

(2) The Federal Plant Pest Act (FPPA) and the Plant Quarantine Act (PQA) allow USDA to regulate "the movement into and through the United States of plants, plant products, plant pests, and any product or article which may contain a plant pest at the time of movement." [154] These articles are regulated in order to prevent the introductions of plant pests that are new to or not widely prevalent in the United States. The Plant Pest Act contains a permit system that could be adapted to form a pre-release review of certain genetically-engineered organisms. However, the Act's jurisdiction presently does not extend to intrastate movement of organisms. Most importantly, these statutes do not apply to genetically-engineered organisms that are not plant pests, thereby exempting a large category of organisms from USDA review.

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[144] 44 Fed. Reg., at 23994 "Policy Statement on Biorational Pesticides."
[145] 49 Fed. Reg., at 50856.
[146] A table summarizing the review requirements applicable to different types of organisms is contained in Appendix E of this report.
[147] *See* Appendix A for a discussion of EPA's review of the Monsanto application.
[148] 21 U.S.C. 151–158.
[149] 7 U.S.C. 150aa–150jj.
[150] 7 U.S.C. 151–164.
[151] 7 U.S.C. 147a.
[152] 7 U.S.C. 2801 *et. seq.*
[153] *See* discussion of jurisdiction, *supra,* Part III, Chapter Three.
[154] 7 U.S.C. 150aa and 151.

USDA asserts that it can regulate the movement of an organism suspected, but not proven, to be a plant pest.[155] Several witnesses at the hearing disputed this by arguing that the statute's scheme allows USDA to regulate only organisms that USDA has determined *can* injure plants.[156]

(3) The Noxious Weed Act gives USDA authority "to regulate the importation or movement interstate of noxious weeds . . ." [157] However, to be regulated as a noxious weed, an organism must be specifically identified in a regulation promulgated after public notice and public hearings. The Secretary must also determine not only that the plant is within the definition of a noxious weed, but that its dissemination may reasonably be expected to have, to a serious degree, a harmful effect. These requirements undermine the usefulness of the Act to review planned releases of genetically-engineered plants.

D. Summary

EPA may require a permit under FIFRA to release genetically-engineered pesticides into the environment. However, it must rely on "notification" and "reporting" under TSCA and has the burden to show, within statutory deadlines, that a biotechnology product is unsafe. Thus, there is a concern that TSCA may prove to be an ineffective statute for the regulation of biotechnology.

USDA's reliance on existing statutes for the regulation of biotechnology has been criticized because the statutes are predominantly remedial in nature, rather than preventive and, thereby, do not provide sufficient authority for pre-release review of genetically-engineered organisms. Those statutes that are, or have the capacity to be, preventive are not presently being enforced with an eye to the potential risks posed by genetically-engineered organisms. For instance, USDA's policy statement does not make clear that review of genetically-engineered organisms under the VSTA will be expanded to consider the ecological safety of releasing the organism. Under the Plant Pest Act, USDA has taken the position that "genetically-engineered organisms which are engineered from certain organisms which are not plant pests or classified in TSCA which do not contain plant pests need not be regulated." [158] This ignores genetically-engineered organisms that are not plant pests, but which may threaten the environment in other ways.

The concerns about the adequacy of USDA's statutory authority to regulate biotechnology go to the primary mandate of USDA itself. While USDA is subject to NEPA, its primary mandate is to "protect and enhance agriculture and forestry in the United States." [159]

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[155] *See* Appendix G, *infra,* Memorandum from John Golden, Assoc. Gen. Counsel to Alan Tracy, Acting Assistant Secretary, Marketing and Inspection Services, June 25, 1985.

[156] *See* Godown testimony and Mellon testimony, *supra,* Part III, Chapter One.

[157] 7 U.S.C. 2801.

[158] 51 Fed. Reg. at 23342.

[159] *Id.*

PART IV

FINDINGS AND RECOMMENDATIONS

Based on documents obtained by the Subcommittee and testimony presented at the various hearings discussed above, the Subcommittee makes the following findings and recommendations:

General

Finding 1. Genetic engineering has enormous potential to fight disease, pollution and hunger. The development of this enabling technology will allow society to use safe genetically-engineered organisms in place of many harmful chemicals in use today.

It is important to retain the competitive advantage the United States presently enjoys in the development of biotechnology, an industry that has enormous possibilities for economic development. Other countries, such as Japan, are targeting biotechnology for increases in research because of its economic potential.

Finding 2. The Federal Government was not fully prepared to review and regulate the first proposal to release genetically-engineered organisms into the environment. Although there have been no known adverse effects on health or the environment from possibly unauthorized releases to date, some of the Federal Government's initial efforts at regulating the first releases of genetically-engineered organisms did not facilitate the commercialization of biotechnology products. Further, some federal and private actions raised public concern regarding the environmental safety of biotechnology. The Coordinated Framework is a significant improvement of the federal regulatory structure for biotechnology.

Finding 3. The NIH Guidelines governing recombinant DNA laboratory research were not intended originally to regulate environmental releases of genetically-engineered organisms. While the caution underlying the NIH Guidelines should be the model for future regulatory systems, there is widespread concern that the Institutional Biosafety Committees, which are used to implement the NIH Guidelines at local research institutions, are not prepared or qualified to implement the Coordinated Framework regulating environmental releases of genetically-engineered organisms.

Recommendation

The GAO should undertake a study of Institutional Biosafety Committees at both public and private institutions. The GAO should evaluate whether these committees, as presently constituted, can adequately perform their oversight role with regard to the environmental release of genetically-engineered organisms. This study should include an evaluation of the diversity of disciplines

presently represented on IBCs, time constraints on IBC review of release proposals, and the consistency of guideline enforcement across institutions and product areas.

Finding 4. A major obstacle to the development of a comprehensive regulatory system is the absence of methodologies to assess the potential risks to the environment posed by the release of genetically-engineered organisms. There is an imbalance between funding (both privately and publicly) for the development of these organisms and funding of risk assessment research. This imbalance threatens to delay the establishment of a general data base on the risks posed by particular types of biotechnology products in various environments.

Recommendation

The BSCC should prepare a plan which identifies gaps in our knowledge about environmental release of biotechnology products, describes ongoing research, and recommends research priorities to address the information gaps. The goal of this plan should be to develop a coordinated and focused research program.

Federal agencies, in cooperation with industry and the university community, should expand research efforts devoted to the development of risk assessment methodologies in order to further their shared interest in the development of a reservoir of knowledge concerning the interaction of genetically-engineered organisms in the environment.

Agencies should promote analysis of risk assessment factors in the early stages of the development of genetically-engineered organisms intended for use in the environment.

Finding 5. Public confidence in the regulatory review process is essential if biotechnology is to achieve its promise. One way to achieve this confidence is for the public to have an opportunity to participate in the review process. Both EPA and NIH provide a 30-day comment period for applications for release into the environment. Presently, the Department of Agriculture system does not provide a comment period. The Department's policy on this subject is inconsistent with the other agencies' policies, and, therefore, does not facilitate efforts to promote public confidence in biotechnology regulation.

Recommendation

The Department of Agriculture should amend its regulations to provide a 30-day public comment period on all regionally or nationally significant commercial or research applications for agriculture permits to release genetically-engineered organisms into the environment.

The Coordinated Framework of June 26, 1986

Biotechnology Science Coordinating Committee

Finding 6. There was general agreement at the hearing that the DPC Working Group and the BSCC had done a good job at admittedly difficult tasks. The Coordinated Framework is noteworthy in

that it addresses, in a comprehensive manner, the regulation of commercial and research products of biotechnology at an earlier stage than has been the case with the regulation of other developing technologies.

The BSCC was envisioned as a coordinating forum for the various agencies involved in the research and development of biotechnology. Recent events, such as the ice-minus case and USDA's licensing of the pseudorabies vaccine, demonstrate the need to coordinate and facilitate the dissemination of technical information related to the federal regulatory system for biotechnology.

Recommendation

The BSCC should promote the development of a system by the agencies for publishing and distributing to local researchers significant general and scientific information related to the Coordinated Framework. The work of NIH's Office of Recombinant DNA Activities (ORDA) in publishing the *Recombinant DNA Technical Bulletin* could serve as a model for this system. The agency representatives to the BSCC should designate staff from within their respective agencies to gather and publish this information and should consider using the Institutional Biosafety Committees at each private and public institution as distribution centers for such information.

Finding 7. Some testimony at the hearings reflected concern regarding the degree to which the BSCC could go beyond its coordinating role and set regulatory policy. The members of the BSCC were encouraged at the hearings to distinguish clearly between their coordinating role on the BSCC and their policy-making responsibilities as members of the Domestic Policy Council Working Group on Biotechnology.

Recommendation

The BSCC should continue to adhere to its role as a coordinating forum. The BSCC should promote interagency cooperation and coordination in open sessions where possible.

Decisions with regulatory impacts should be made by the agencies and should involve the public at the earliest opportunity.

Finding 8. Key terms such as "release into the environment" and "contained facility" have not been defined in the Coordinated Framework, leaving each agency to impose and enforce their own definitions for those terms; this may result in inconsistencies which could hamper the implementation of the Coordinated Framework.

The BSCC intends to complete its work through the efforts of subcommittee working groups. However, a rigorous schedule for completion of this work is needed to clarify these important regulatory issues.

Recommendation

The BSCC should expedite the work of its subcommittee working groups in order to complete the implementation of the Coordinated Framework. The BSCC should require completion of the working group studies within six months of this report.

The BSCC should encourage the agencies to give first priority to the promulgation of all rules necessary to implement the Coordinated Framework.

Finding 9. User fees could help ensure that the regulatory agencies have adequate resources to conduct their regulatory reviews. The Administration has not developed a consistent policy towards the imposition of user fees for review of biotechnology products. Dr. Kingsbury testified that the BSCC has not considered user fees in its discussions.

Recommendation

The administration should prepare a report to Congress which reviews its position on the imposition of user fees for review of biotechnology products. The report should analyze the adequacy of existing budgets for review of biotechnology products. The report also should evaluate whether it is appropriate to differentiate user fees based on the size or income of biotechnology companies, and what effect this would have on their ability to compete.

DEFINITIONS

Finding 10. The definitions contained in the Coordinated Framework will have significant regulatory impact by determining what level of review different classes of organisms will receive prior to their use in the environment. The definitions delineate categories of organisms by the genetic material used to construct them. There is concern that this system of evaluating risks by examining only the nature of the finished product is incomplete because it does not take into consideration the potential risks that these new organisms may pose in a particular environment.

Organisms that have received genetic material from different genera or from pathogenic source organisms receive the highest level of review under the Coordinated Framework. However, organisms that have received only non-coding regulatory sequences from different genera are not considered "intergeneric organisms", and organisms considered to be "opportunistic pathogens" are not classified as "pathogenic organisms", and are not considered *a priori* to pose as high a degree of potential risk for health and the environment; therefore, they receive a lower level of review prior to introduction into the environment. Several scientists testified at the Hearing on the Coordinated Framework for Regulation of Biotechnology that these exclusions raise serious questions because, in some cases, organisms with altered non-coding regulatory sequences may differ substantially from their unaltered form.

Recommendation

The BSCC should re-evaluate which organisms are excluded from the definitions of "intergeneric organisms" and "pathogens." Specifically, the BSCC should reconsider excluding from those definitions opportunistic pathogens and organisms containing any alteration (addition or deletion) of non-coding regulatory sequences.

JURISDICTION

Finding 11. The Coordinated Framework replaces an uncoordinated regulatory approach with a system that may have the potential for redundant and inconsistent review—by agencies with different levels of regulatory authority—of proposals to release genetically-engineered organisms into the environment. Although the agencies intend to clarify the situation through Memoranda of Understanding, how these agreements will be implemented on a day-to-day basis remains unclear.

Recommendation

Agencies funding research proposals involving the release into the environment of genetically-engineered organisms should inform the grantee of the applicable regulatory path for such releases at the time the grant is awarded.

Jurisdiction to review such research proposals should be established at the time of awarding the research grant rather than at the time of application to release the genetically-engineered organism. The agency of jurisdiction should communicate its regulatory requirements to principal investigators at the earliest opportunity.

Jurisdiction to review commercial applications for the release of genetically-engineered organisms into the environment should be established upon receipt of the application.

AUTHORITY

Finding 12. In order to protect health and the environment, the agencies' authority to review and, if necessary, prevent, releases of genetically-engineered organisms into the environment must be commensurate with the potential risks such organisms pose. The Coordinated Framework takes the approach that intergeneric organisms and organisms derived from pathogenic source organisms pose the greatest potential risks and therefore should receive full scientific review prior to their introduction into the environment. Dr. Kingsbury testified that the statutes cited in the Coordinated Framework, when taken collectively, provide adequate authority to review all potentially harmful genetically-engineered organisms prior to their release into the environment.

Some witnesses were concerned that the individual statutes the agencies rely upon under the Coordinated Framework do not provide for full review of this high-risk category of organisms. Under FIFRA, EPA requires a permit before such organisms are released. Under TSCA, EPA cannot require a permit and has the burden to show, within statutory deadlines, that a product is unsafe. USDA, under the Federal Plant Pest Act, may require a permit for release of a "plant pest." However, USDA has no authority to require a permit prior to release of an intergeneric organism that has been proven not to be a plant pest but has the potential to pose other environmental problems.

TSCA may be sufficient for regulation of those categories of genetically-engineered organisms which EPA considers to pose little risk. However, it is unclear whether TSCA's rulemaking provisions can be effectively utilized to regulate genetically-engineered organisms formed from intergeneric material or pathogenic source or-

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ganisms. It is conceivable that when the agency has to process only a few applications, it may be able to promulgate rules in an efficient manner. However, should the number of applications significantly increase, it is questionable whether the agency would have adequate resources to manage the regulatory burden.

In some cases, USDA's review of specific products under statutes it administers has been inconsistent. This results in part from USDA's reliance on remedial statutes such as the Plant Pest Act, for preventive actions. Statutes such as the Noxious Weed Act and the Plant Quarantine Act appear to be deficient in authority to serve preventive purposes.

Recommendation

The Coordinated Framework considers intergeneric organisms and pathogens to pose the greatest potential risks to health and the environment. In order to accommodate full scientific review of intergeneric organisms and pathogens prior to their release into the environment, the head of each agency regulating these products should require permits for their release, using existing statutory authority where available, and should seek additional permitting authority from the Congress where necessary.

USDA should promulgate regulations as soon as possible that detail how the Department will apply the Federal Plant Pest Act and the Plant Quarantine Act to the regulation of environmental release of genetically-engineered organisms that are intrageneric or non-pathogenic.

USDA

Finding 13. Genetic engineering holds great potential for agriculture. A significant proportion of genetically-engineered organisms will have agricultural purposes. This places a heavy burden on USDA to develop and implement a clear system for the review, assessment, and regulation of agricultural biotechnology products. While all agencies are subject to NEPA, USDA's primary mandate is to protect and promote agriculture and forestry. This has led to criticism of USDA's approach to the potential risks posed by the environmental release of genetically-engineered organisms.

A GAO study of USDA's biotechnology regulatory structure, commissioned by the House Committee on Science and Technology, concluded that USDA's regulatory system needed clarification and made specific recommendations to the Secretary of Agriculture. The Subcommittee on Investigations and Oversight concurs in the findings of the GAO report, and while the Subcommittee recognizes USDA's efforts to address these concerns, the Subcommittee believes that USDA's actions to date have not fully addressed the issues and recommendations of the GAO report.

Recommendations

As the GAO recommended, USDA should:

Provide the Agricultural Recombinant DNA Research Committee (or a future central committee within the USDA) with the authority and sense of direction it needs

to act efficiently as the Department's focal point for biotechnology.

Look for and take advantage of opportunities to improve and increase the communication of USDA's views concerning biotechnology, both in terms of the benefits to be derived and the risks that must be considered and managed.

USDA should implement a biotechnology regulatory system that will identify the Department's regulatory path for licensing biotechnology products and approving requests involving releases of genetically-engineered organisms into the environment.

Finding 14. The Science and Education Division, which oversees USDA-funded biotechnology research, has not consistently promoted risk assessment research geared to the specific hazards posed by the environmental release of genetically-engineered organisms whose development the Department is funding.

Recommendation

At the earliest time that a research proposal is known to lead to the release into the environment of a genetically-engineered organism, USDA should act to make the assessment of risks a part of that research proposal.

Finding 15. The Marketing and Inspection Division, which has regulatory authority over products required to be submitted to USDA for licensing or dissemination, has not taken full advantage of the biotechnology expertise represented on the Agricultural Recombinant DNA Research Committee (now the ABRAC) within the Science and Education Division in reviewing the potential risks posed by genetically-engineered products regulated by the Marketing and Inspection Division. Testimony indicates that, based on previous experience, Marketing and Inspection's review of genetically-engineered organisms may often, as a rule, not require the submission of "new" data and may be expected to take only ten days. The Subcommittee is concerned that this system may not implement the review standards described in the Coordinated Framework.

Recommendation

USDA should implement immediately an organized process for incorporating into its regulatory system scientific expertise located throughout the Department and, where appropriate, located in the private sector.

In addition to its responsibilities under NEPA, where appropriate, USDA should include in its review of organisms proposed for release into the environment an evaluation of the organisms's potential impact on the environment. USDA's review of the potential hazards posed by novel organisms should be based on case specific data and a high level of interaction with the applicant.

Finding 16. One of the reasons the Marketing and Inspection Division cites for not systematically consulting the Science and Education Division in reviewing new products is that the Science and Education Division's review process may jeopardize confidential

business information submitted by license applicants. The Marketing and Inspection Division's concerns are an exception to the experience of other agencies that have used outside advisors to review product applications containing confidential business information and by the Trade Secrets Act which establishes the obligation of all federal employees to safeguard confidential business information.

Recommendation

USDA should implement Department-wide standards for the handling of confidential business information, thereby enabling it to fully utilize scientific expertise existing throughout the Department to evaluate applications to release genetically-engineered organisms.

EPA

Finding 17. In contrast to USDA, EPA's primary mission is to protect the environment as a whole. EPA's efforts at regulating genetically-engineered pesticides evidences awareness of the potential risks posed by genetically-engineered organisms. EPA's interim policy under FIFRA for the regulation of genetically-engineered pesticides is commendable for its cautious approach. However, the data requirements under the proposed Level I and Level II reviews appear to be ambiguous and may lead to unnecessary delays in reviewing FIFRA applications.

EPA's implementation of TSCA will be incomplete and will be based on voluntary compliance until EPA promulgates rules: (1) defining significant new uses; (2) removing the pre-manufacture notification exemption for research and development activities; (3) applying reporting requirements to certain field experiments; and (4) redefining "small business".

Recommendation

EPA should clarify its regulatory process under FIFRA by establishing consistent data reporting requirements for microbial pesticides. Review of such data should be based on well defined terms and, in the case of field test sites, direct observation where appropriate.

EPA should expedite the promulgation of all rules necessary for TSCA to regulate the environmental release of certain genetically-engineered organisms.

INDUSTRY

Finding 18. The biotechnology industry's record of compliance with applicable regulatory guidelines for laboratory research with, and planned releases of, genetically-engineered organisms is commendable. Those few violations of the guidelines that have occurred share a common theme—the failure of individual scientists to exercise good judgment before carrying out field tests with genetically-engineered organisms. In both the ice-minus case and the pseudorabies vaccine case, the scientists should have confirmed their interpretation of the guidelines involving recombinant DNA research with appropriate local and federal authorities.

The industry is showing a commendable and heightened awareness of the need to inform the public of the nature and purpose of proposed outdoor experiments with genetically-engineered organisms.

APPENDIX A

The First Proposals to Release Genetically-Engineered Organisms Into the Environment: A Summary*

1. AGRACETUS

In May 1983, Agracetus, on its own initiative, asked NIH to review its plan to field test a strain of tobacco which has been genetically-engineered to be resistant to a specific disease. The company voluntarily asked NIH to review its proposal because NIH was the only federal agency with expertise and experience in evaluating recombinant DNA research at the time, and the company felt the review of their proposal would allay public concerns about the risks posed by release of genetically-engineered organisms.

However, a lawsuit which Jeremy Rifkin brought against the NIH Recombinant DNA Advisory Committee (RAC) in 1984 enjoined NIH/RAC from approving the field test of any genetically-altered organisms without conducting an environmental assessment (see discussion on Advanced Genetic Systems, next).

Agracetus subsequently submitted its application to APHIS. In June 1985, APHIS wrote to Agracetus, saying that the genetically-engineered tobacco plant posed "no problem" for release, as it was not a plant pest. This, according to a company spokesperson, placed a large share of the responsibility for the release on the company. A company official told a GAO investigator that his company was left somewhat in a quandary by the APHIS letter, and, as a result, had decided to hold off the intended tobacco planting for another year. (The Company had already held off planting for two seasons.)

Essentially, USDA decided not to get involved in regulating the Agracetus case and Agracetus turned once again to the NIH/RAC. On November 13, 1985, the plan to plant the genetically-altered tobacco plant in an experimental field was approved by the NIH/RAC. Agracetus announced on May 31, 1986, that it had planted a test plot of the plants in Wisconsin.

2. ADVANCED GENETIC SCIENCES (AGS) AND THE UNIVERSITY OF CALIFORNIA, BERKELEY

In 1983, Steven Lindows of the University of California submitted a research proposal to the NIH/RAC which involved the intentional release of a genetically-altered strain of bacteria, whose purpose is to prevent frost damage to crops (called the "ice-minus" strain of bacteria). NIH/RAC approved Lindows' plan to spray this organism on a field of potato plants in May, 1984. However, the lawsuit brought by Jeremy Rifkin enjoined the field test, on the ground that an adequate environmental assessment study had not been conducted by NIH/RAC.

Advanced Genetic Sciences, the corporation which funded Lindow's research at the University of California subsequently submitted a proposal to EPA for approval of the application of the "ice-minus" bacteria to strawberry plants. On November 14, 1985, EPA, under the authority of FIFRA, approved AGS' experimental use permit (EUP). However, in March 1986, EPA learned, through its own investigation and through testimony before the Investigations and Oversight Subcommittee, that AGS had conducted unauthorized, uncontrolled experiments with the bacteria on the rooftop of its office building. EPA withdrew AGS' EUP and instigated administrative proceedings against AGS for violations of FIFRA. They were fined $20,000, the maximum allowable by law. Subsequently, Monterey County, the site of the proposed field test put a moratorium on the test at

least through the end of 1986. In a settlement reached between AGS and EPA, the fine was reduced to $13,000 for failing to adequately report the experimental design and methodology for studies submitted to support the EUP.

Meanwhile, in December of 1985, Steven Lindows submitted his EUP application to field test "ice-minus" on potato plants to EPA. On May 13, 1985, EPA approved the permit application. Jeremy Rifkin has formally requested that the University of California withdraw approval of the experiment after July 1 on the grounds that the university system is losing liability insurance covering sudden accidents that result in either pollution or contamination of the environment or injury to public health as of that date, and that they have been unable to secure liability coverage from any commercial insurance source after that date. Mr. Rifkin's group, the Foundation on Economic Trends, has announced their intention to sue EPA for authorizing this experiment before an adequate review of insurance liability questions and unresolved safety issues were undertaken.

Local citizen opponents of the field test, along with Jeremy Rifkin have obtained a court order delaying the test. In an out of court settlement, reached in August, 1986, the university agreed to postpone the test at least until next year, meet with opponents to discuss their concerns, and conduct an assessment to determine whether a full environmental impact report is needed.

3. MONSANTO

Monsanto notified EPA in early 1985 of its desire to conduct a field test on a microbial pesticide. They have inserted a Bacillus thuringiensis toxin gene, which specifically protects corn plants from damage due to root worms, into the Pseudomonas bacteria. EPA reviewed the data submitted by the company, and in March, 1985 requested that the company perform additional tests in order to obtain an EUP. In April, 1986 the Scientific Advisory Panel of experts convened by EPA to review Monsanto's data, advised EPA that the company should be allowed to proceed with the field test. However, EPA's own internal scientists decided that more data would be required from Monsanto and that certain tests needed to be repeated. The company has agreed to comply with EPA's request, but they have missed this growing season and will have to wait for next year. They have stated that they may or may not proceed with the test. The St. Charles County Council (Missouri), was prepared to block the test based on the fact that the test site was in a flood plane.

4. CALGENE

Calgene has developed an herbicide-resistant strain of tobacco and has applied for USDA approval to field test. It is noteworthy that Calgene submitted its application to the Secretary of USDA rather than APHIS. (Agracetus, in contrast, asked APHIS to review its disease resistant strain of tobacco). This was due to the confusion at the time, about how to make an application of this nature to USDA. Calgene temporarily suspended its application to await USDA's new policy guidelines and organizational structure for biotechnology product review approval before submitting additional data for an EUP.

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* Prepared by the Investigations and Oversight Subcommittee.

Appendix B

APPLICATIONS TO RELEASE GENETICALLY-ENGINEERED ORGANISMS APPROVED BY EPA*

Experimental Use Permits Required

1. **Dr. Steven Lindows**, University of California/Berkeley -- Ice-minus (Pseudomonas syringae)

2. **Advanced Genetic Sciences, Inc.**, Oakland, California -- (Pseudomonas syringae and Pseudomonas fluorescens) EPA suspended the EUP pending the following:

   A) AGS must repeat the pathogenicity tests on certain fruit trees. (AGS has repeated the tests and determined that the parent and engineered derivative of both strains are not pathogenic.)

   B) AGS must inform EPA of the location of their new field test site. The Agency will determine if the site is acceptable.

3. **Monsanto**, St. Louis, Missouri -- (Pseudomonas flourescens containing toxin gene from Bacillus thuringiensis) EPA informed Monsanto that they need to submit additional data to support their EUP application.

No Experimental Use Permit Required

(Submitted notification and EPA determined that an EUP was not necessary)

1. **Ecogen, Inc.**, Langhorne, Pennsylvania -- Bacillus thuringiensis

2. **Professor David Sands**, Montanta State University/Bozeman -- Sclerotinia sclerotiorum

3. **Dr. Gary Harmon**, Cornell University -- Trichoderma harzianum

*Based on information provided by Fredrick Betz, Hazard Evaluation Division, Office of Pesticide Programs, EPA (September 12, 1986).

DEPARTMENT OF AGRICULTURE
OFFICE OF THE SECRETARY
WASHINGTON, D.C. 20250

August 15, 1986

Honorable Don Fuqua
Chairman
Committee on Science and
Technology
U.S. House of Representatives
Washington, D.C. 20515

Dear Congressman Fuqua:

This responds to your written request of August 15, 1986 for a list of applications on genetically engineered organisms currently pending before the U.S. Department of Agriculture

Enclosed please find such a list of products provided by the Animal and Plant Health Inspection Service (APHIS). Some of this information may fall within the coverage of the Trade Secrets Act (18 U.S.C. 1905), and we request that the Committee and staff treat the information consistently with the protections afforded by that Act.

In addition to these products, the Department has also received and reviewed a request from Calgene, Inc. to field test tobacco plants that are herbicide resistant. Contrary to what I told one of your staff members on the phone August 14, this review has been put on hold at Calgene's request.

If you have any further questions, please feel free to contact me at 447-9277.

Sincerely,

Daniel D. Jones

Daniel D. Jones, Ph.D.
Interim Deputy Director
Office of Agricultural Biotechnology

Enclosure

cc: J. Glosser, APHIS
O. Bentley, S&E

United States Department of Agriculture
Animal and Plant Health Inspection Service
Washington, DC 20250

CONFIDENTIAL

August 4, 1986

SUBJECT: Notification of Submissions--
Genetically Engineered Organisms

TO: Orville G. Bentley
Assistant Secretary
Science and Education

This memorandum updates the notifications supplied by the Animal and Plant Health Inspection Service (APHIS) on June 2, July 21, and July 22, 1986.

Pursuant to the authority granted by the Federal Plant Pest Act, as amended (7 U.S.C. 150aa-150jj), the following submissions for genetically engineered organisms have been submitted directly to Plant Protection and Quarantine, APHIS:

000018 - field test of a nongenetically engineered herbicide tolerant crop plant*
000019 - field test genetically engineered tobacco plant-crown gall
000021 - field test genetically engineered herbicide tolerant tobacco plant
000024 - field test genetically engineered herbicide tolerant tobacco plant
000030 - in vitro cloned maize streak virus DNA (in containment)
000033 - permit to import genetically engineered potato plant material

Pursuant to the authority granted by the Virus-Serum-Toxin Act (21 U.S.C. 151-158), and the licensing provisions found in the pertinent regulations at 9 CFR 102, APHIS' Veterinary Services (VS) currently has on file in the Veterinary Biologics Staff the following recombinant-derived applications:

1891.RO - pseudorabies vaccine, modified live virus, single gene deletion, for use in swine

1891.RI - pseudorabies vaccine, modified live virus, double gene deletion, for use in swine

Submissions listed by accession number and product code contain trade secret and confidential commercial information and are processed in conformance with the APHIS requirements for the control and protection of confidential business information (CBI) published at 50 FR 38561-63 on September 23, 1985. Trade secret, secret, and confidential business information is exempt from disclosure under section (b)(4) of the Freedom of Information Act (5 U.S.C. 552(b)(4)), and thus any request for additional information about the submissions accorded accession numbers or product codes should be made in conformance with section VIII of the APHIS CBI requirements.

The submission marked with an asterisk has been reviewed and approved by APHIS.

Please note that two accession numbers previously reported on July 21 do not appear on this updated list. Accession number 000025 was not produced by recombinant techniques, and 000026 was withdrawn. Two product codes previously reported on July 22, 14R1.20 and 26R8.62, were deleted from this notification because the applications do not involve recombinant techniques.

Bert W. Hawkins
Administrator

Table 1c

Company activities in biotechnology—specialty chemicals

Company	Partner	Program
Amgen	Texaco	Family of Specialty Chemicals
none	Indigo	
Bio-Response	U.S. Army	Neurotransmitter Agents
Genentech	Pfizer	Vitamin C
Genencor	Genentech / Corning Glass Works / A.E. Staley	Subtilisin
Genetics Institute	Gist Brocades	Not announced
	ChemDesign	Specialty diol
	none	L-amino acids by transamination
	International Paper	Unnamed specialty chemical
	none	L-aspartic acid
	none	Enzyme engineering project 1
	none	Enzyme engineering project 2
Genex	Lark SPA	Unnamed Specialty Chemical Intermediate
Gist-brocades	none	Chymosine
Kyowa Hakko	none	5'—guanyl acid (food seasoning
RepliGen	Cellulose du Pin	Pulp and paper enzymes
	FMC	Pesticides
	none	Chemical Waste Detoxification
	none	Biofouling control systems
	none	Plant antiviral compounds
Synergen	Getty Scientific	Enhanced oil recovery chemicals
	Ganes Chemical	Pharmaceutical intermediate
	Eli Lilly	Process enzymes
Ube Industries	none	Pyrrolo-quinoline quinone (vitamin)

From Biotechnology Industry- 1986 Fact Book, compiled by PaineWebber, Linda I. Miller, CFA

Table 17
Competitive status of biotechnology programs—agriculture

Product	Company	Commercial Partner	Status
		Alfalfa	
Alfalfa	Plant Genetics	not available	not available
		Barley	
Malting barley varieties	Sungene Technologies	Great Western Maltng	Preliminary field testing
		Cocoa	
Improved Cocoa Flavor	DNA Plant Technology	Hersney	not available
		Coffee	
Coffee	Native Plants	Kyowa Hakko/Sumitomo	not available
Coffee	DNA Plant Technology	General Foods	not available
		Corn	
High Tryptophan corn	Molecular Genetics	none	Field development
High Amino Acid Corn	Molecular Genetics	none	Field development
High Oil Corn	Sungene Technologies	Mitsubishi	Preliminary field testing
High Yielding Corn	Sungene Technologies	none	Advanced field testing
Microbially Improved High Yielding Corn	Agracetus	Cetus/W.R. Grace	not available
Herbicide Tolerant Corn	Calgene (glyphosate)	DeKalb (Pfizer)	Research
	Molecular Genetics	American Cyanamid Pioneer Hybrid	Field development
Improved Corn Varieties	Genetics Institute	United AgriSeeds	not available
Insect Resistant Corn	Agracetus	Cetus/W.R. Grace	not available
Improved Popcorn	DNA Plant Technology	American Home Products	not available
		Cotton	
Insect Resistant Cotton	Agracetus	Cetus/W.R. Grace	not available
		Rape Seed	
Herbicide Tolerant Rape Seed	Calgene (phenmedipham)	Kemira Oy	not available
		Soybean	
Soybeans	Calgene	Nestle	not available
	Genetics Institute	none	not available
Insect Resistant Soybeans	Agracetus	Cetus/W.R. Grace	not available
Microbially Improved High Yielding Soybeans	Agracetus	Cetus/W.R. Grace	not available
Rhizobium for Soybean Nitrogen Fixation	Agracetus	Cetus/W.R. Grace	not available
		Sunflower	
Specialty Sunflower Oil Varieties	Sungene Technologies	Lubrizol	Preliminary field testing
Herbicide Tolerant Sunflowers	Calgene (bromoxynil)	Rhone Poulenc	Field trials expected 1987
		Sugar Cane	
Disease Free Sugar Cane	Crop Genetics	none	not available
		Tobacco	
Herbicide Tolerant Tobacco	Calgene (glyphosate)	Koker Seed	First field trials in Spring 1986
Cigarette Tobacco	Calgene	not disclosed	Research

Table 1

Product	Company	Commercial Partner	Status
		Tomatoes	
Process Tomatoes	Calgene	Campbell Soup	Research
Tomatoes with high Solid Content	DNA Plant Technology	Campbell Soup	not available
		Flavors and Fragrances	
Plant derived Flavors and Fragrances	DNA Plant Technology	Firmenich	not available
		Nursery Plants	
Artificial Nursery Products	Plant Genetics	Kirin Brewery (Japan)	not available
	Twyford Plant Laboratories	Nissho Iwai (Japan)	not available
Cell Fusion technology	Chugai Pharmaceutical (Japan)	South Carolina College of Medicine	not available
		Poplar and Pine	
Herbicide Tolerant Poplar and Pine	Calgene (glyphosate)	U.S. Forest	Field trial application 1986
		Palm Trees	
Cloning Oil Palm Trees	DNA Plant Technology	United Fruit Company	not available
		Pesticides	
Insecticides	Genetics Institute	none	not available
	Mycogen	not available	not available
Nematocide	Genetics Institute	not announced	not available
	Synergen	none	Research
		Other	
Agriculture/Chemical Plant Interactions	Sungene Technologies	FMC	Laboratory research
Herbicide Tolerant Crops	BioTechnica International	BioTechnica Limited BioTechnica International of Canada	not available
Ice Nucleation Bacteria	Advanced Genetic Sciences	none	not available
Microbial Pesticides	BioTechnica International	Monsanto	not available
Plant Oils	Calgene	Not disclosed	not available
Plant Oils	Calgene	Not disclosed	not available
Rhizobium	BioTechnica International	none	Greenhouse trials
Seeds	Sungene Technologies	Mitsubishi (Japan)	not available
Silage inoculum	BioTechnica International	none	Supposite to be marketed in 1986
Stress tolerance	Calgene	Roussel Uclaf	not available

APPENDIX C

CHART I -- COORDINATED FRAMEWORK --
APPROVAL OF COMMERCIAL BIOTECHNOLOGY PRODUCTS

Subject	Responsible Agency(ies)
Foods/Food Additives	FDA*, FSIS[1]
Human Drugs, Medical Devices and Biologics	FDA
Animal Drugs	FDA
Animal Biologics	APHIS
Other Contained Uses	EPA
Plants and Animals	APHIS*, FSIS[1], FDA[2]
Pesticide Microorganisms Released in the Environment	
All	EPA*, APHIS[3]
Other Uses (Microorganisms)	
Intergeneric Combination	EPA*, APHIS[3]
Intrageneric Combination	
Pathogenic Source Organism	
1. Agricultural use	APHIS
2. Non-Agricultural use	EPA*[4], APHIS[3]
No Pathogenic Source Organisms	EPA Report
Nonengineered Pathogens	
1. Agricultural Use	APHIS
2. Non-agricultural Use	EPA*[4], APHIS[3]
Nonengineered Nonpathogens	EPA Report

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* LEAD AGENCY

1 FSIS, Food Safety and Inspection Service, under the Assistant Secretary of Agriculture for Marketing and Inspection Services is responsible for food use.

2 FDA is involved when in relation to a food use.

3 APHIS, Animal and Plant Health Inspection Service, is involved when the microorganism is plant pest, animal pathogen or regulated article requiring a permit.

4 EPA requirements will only apply to environmental release under a "significant new use rule" that EPA intends to propose.

(51 FR 23302 at 23304)

CHART II--COORDINATED FRAMEWORK--BIOTECHNOLOGY RESEARCH JURISDICTIO

Subject	Responsible Agency(ies)
Contained Research, No Release in Environment	
1. Federally Funded	Funding agency[1]
2. Non-Federally Funded	NIH or S&E voluntary review, APHIS[2]
Foods/Food Additives, Human Drugs, Medical Devices, Biologics, Animal Drugs	
1. Federally Funded	FDA*, NIH guidelines & review
2. Non-Federally Funded	FDA*, NIH voluntary review
Plants, Animals and Animal Biologics	
1. Federally Funded	Funding agency*[1], APHIS[2]
2. Non-Federally Funded	APHIS*, S&E voluntary review
Pesticide Microorganisms	
Genetically Engineered	
Intergeneric	EPA*, APHIS[2], S&E voluntary review
Pathogenic Intrageneric	EPA*, APHIS[2], S&E voluntary review
Intrageneric Nonpathogen	EPA*, S&E voluntary review
Nonengineered	
Nonindigenous Pathogens	EPA*, APHIS
Indigenous Pathogens	EPA*[3], APHIS
Nonindigenous Nonpathogen	EPA*,
Other Uses (Microorganisms) Released in the Environment	
Genetically Engineered	
Intergeneric Organisms	
1. Federally Funded	Funding agency*[1], APHIS[2], EPA[4]
2. Commercially Funded	EPA, APHIS, S&E voluntary review,
Intrageneric Organisms	
Pathogenic Source Organism	
1. Federally Funded	Funding agency*[1], APHIS[2], EPA[4]
2. Commercially Funded	APHIS*[2], EPA (*if non-agricul. use)
Intrageneric Combination	
No Pathogenic Source Organisms	EPA Report
Nonengineered	EPA Report*, APHIS[2]

* LEAD AGENCY

1 Review and approval of research protocols conducted by NIH, S&E, or NSF.

2 APHIS issues permits for the importation and domestic shipment of certain plants and animals, plant pests and animal pathogens, and for the shipment or release in the environment of regulated articles.

3 EPA jurisdiction for research on a plot greater than 10 acres.

4 EPA reviews federally funded environmental research only when it is for commercial purposes.

(51 FR 23302 at 23305)

APPENDIX D

CHARTER

BIOTECHNOLOGY SCIENCE COORDINATING COMMITTEE OF THE FEDERAL COORDINATING COUNCIL FOR SCIENCE, ENGINEERING, AND TECHNOLOGY

PURPOSE

The Domestic Policy Working Group on Biotechnology has determined that in the area of biotechnology with its rapid growth of scientific discovery, scientific issues of interagency concern will arise frequently and need to be communicated among the various agencies involved with reviews of biotechnology applications. The Federal Coordinating Council for Science, Engineering, and Technology (FCCSET) established by 42 U.S.C. 6651 is an interagency science committee chaired by the Director of the Office of Science and Technology Policy with the mission of coordinating science activities affecting more than one agency. Committees may be established under FCCSET for addressing particular science issues. Thus, the Biotechnology Science Coordinating Committee (BSCC) is established to provide formally an opportunity for interagency science policy coordination and guidance and for the exchange of information regarding the scientific aspects of biotechnology applications submitted to federal research and regulatory agencies for approval.

FUNCTIONS

The BSCC will coordinate interagency review of scientific issues related to the assessment and approval of biotechnology research applications and biotechnology product applications and post-marketing surveillance when they involve the use of recombinant RNA, recombinant DNA, cell fusion or similar techniques. The BSCC will:

(a) Serve as a coordinating forum for addressing scientific problems, sharing information, and developing consensus;

(b) Promote consistency in the development of Federal agencies' review procedures and assessments;

(c) Facilitate continuing cooperation among Federal agencies on emerging scientific issues; and,

(d) Identify gaps in scientific knowledge.

AUTHORITY

To accomplish these functions the BSCC is authorized to:

(a) Receive documention from agencies necessary for the performance of its functions;

(b) Conduct analyses of broad scientific issues that extend beyond those of any one agency;

(c) Develop generic scientific recommendations that can be applied to similar, recurring applications;

(d) Convene workshops, symposia, and generic research projects related to scientific issues in biotechnology; and

(e) Hold periodic public meetings.

MEMBERS AND CHAIRMAN

The BSCC includes the following initial members:

Department of Agriculture
- Assistant Secretary for Marketing and Inspection Services
- Assistant Secretary for Science and Education

Department of Health and Human Services
- Commissioner Food and Drug Administration
- Director National Institutes of Health

Environmental Protection Agency
- Assistant Administrator for Pesticides and Toxic Substances
- Assistant Administrator for Research and Development

National Science Foundation
- Assistant Director for Biological, Behavioral & Social Sciences

The BSCC is chaired by the Assistant Director for Biological, Behavioral and Social Sciences of the National Science Foundation and the Director of the National Institutes of Health on a rotating basis.

ADMINISTRATIVE PROVISIONS

(a) The BSCC will report to FCCSET through the Chair.

(b) Meetings of the BSCC shall be held periodically. Some public meetings will be held.

(c) Confidential business information and proprietary information shall be protected under the confidentiality requirements of each member agency.

(d) Subcommittees and working groups, with participation not restricted to BSCC members or full-time Federal employees, may be formed to assist the BSCC in its work.

(e) All BSCC members will be full-time Federal employees whose compensation, reimbursement for travel expenses and other costs shall be borne by their respective agencies.

(f) Each member of the BSCC shall provide such agency support and resources as may be available and necessary for the operation of the BSCC including undertaking special studies as come within the functions assigned herein.

(g) An Office of Science and Technology Policy staff member will serve as BSCC Executive Secretary.

DURATION

The BSCC shall continue for a period of two years at which time the continuing need for the BSCC will be reviewed prior to its renewal.

DETERMINATION

I hereby determine that the formation of the BSCC is in the public interest in connection with the performance of duties imposed on the Executive Branch by law, and that such duties can be best performed through the advice and counsel of a such a group.

Approved:

October 30, 1985
(Date)

G.A. Keyworth, II, Chairman
Federal, Coordinating Council
for Science, Engineering and
Technology

BIOTECHNOLOGY SCIENCE COORDINATING COMMITTEE
OF THE
FEDERAL COORDINATING COUNCIL
FOR SCIENCE, ENGINEERING, AND TECHNOLOGY

AGREEMENT OF THE MEMBERS

The undersigned members of the BSCC, in order to fully participate in the activities of the BSCC, do hereby agree to: expedite all necessary proper agency clearances for other members so that they can receive proprietary and confidential business information; provide a system to fully protect proprietary and confidential business information; provide such agency support and resources as may be available and necessary for the operation of the BSCC; and, to perform such other duties for the operation of the BSCC as may be necessary to carry out the functions described above.

Raymond D. Pitt — 11-13-85
Assistant Secretary for Marketing and Inspection Services, Department of Agriculture — Date

Orville G. Bentley — Nov. 8, 1985
Assistant Secretary for Science and Education, Department of Agriculture — Date

[signature] — NOV 6 1985
Commissioner, Food [illegible] Administration, Department of Health and Human Services — Date

James B. Wyngaarden — Nov 6, 1985
Director, National Institutes of Health, Department of Health and Human Services — Date

[signature] — 8 Nov 1985
Assistant Administrator for Pesticides and Toxic Substances, Environmental Protection Agency — Date

[signature] — 8 Nov 1985
Assistant Administrator for Research and Development, Environmental Protection Agency — Date

David T. Kingsbury — November 6, 1985
Assistant Director for Biological, Behavioral and Social Sciences, National Science Foundation — Date

APPENDIX E

SUMMARY TABLE: PRIOR NOTIFICATION AND REVIEW OF MICROORGANISMS APPLIED IN THE ENVIRONMENT

TYPE OF MICROBIAL PRODUCT	COVERAGE BY NOTIFICATION AND REVIEW POLICY 1/			
	FIFRA		TSCA	
	≤10 acres	>10 acres	≤10 acres	>10 acres
1. Genetically engineered microorganisms				
a. Formed by deliberate combinations of genetic material from dissimilar source organisms (inter-generic combinations)	X	X	X	X
b. Formed by genetic engineering other than inter-generic combinations				
i. pathogenic source organisms 2/	X	X	X	X
ii. nonpathogenic source organisms	O	X	O	O
2. Nonengineered microorganisms				
a. Nonindigenous pathogens 2/	X	X	O	X
b. Nonindigenous nonpathogens	O	X	O	O
c. Indigenous pathogens 2/		X	O	X
d. Indigenous nonpathogens		X	O	O

1/ "X" designates that the microorganism will be subject to EPA review prior to small-scale (10 acres or less) or large scale (greater than 10 acres) environmental applications, as indicated. Under TSCA, submitters would only notify the Agency once (at the first appropriate time), unless during the original review EPA specifies that further reporting is required.

"O" designates that the microorganism will be subject to abbreviated review prior to small-scale (10 acres or less) or large scale (greater than 10 acres) environmental applications, as indicated. Under FIFRA, this provision is effective immediately. Under TSCA, the abbreviated notification will be implemented through rulemaking.

2/ Pathogens in this category used solely for non-pesticidal agricultural purposes will not be subject to EPA notification requirements. They will be subject only to USDA review. See Unit IV for a definition of "agricultural uses" and "pathogens."

(51 FR 23302 at 23319)

APPENDIX F

November 5, 1985

Mr. Thomas C. Bevard
Biologics Corporation
2720 North 84th Street
Omaha, NE 68134

Dear Mr. Bevard:

This is in response to your September 18 and October 14, 1985, submissions requesting additional field trial testing sites for your experimental Pseudorabies Vaccine, Modified Live Virus, Code 1891.RO.

This will confirm verbal authorization of October 28, 1985, to conduct these trials according to your proposed protocol in Illinois and Michigan in accordance with the stipulations in my April 15, 1985, letter.

Our only comment on the proposed field trial experiment is that you are not planning to evaluate this product in 3-day-old animals. You are going to vaccinate only healthy weaned pigs, yet in your Outline of Production, Section VI.D you recommend vaccinating 3-day-old piglets. The safety testing protocol must be expanded to include the young piglet.

Please note the new product code number, Code 1891.RO. This code identifies recombinant derived products from conventional ones. Please make the necessary corrections.

On October 31, 1985, I had a discussion with Dr. Michael J. Bartkoski concerning the general characterization and nature of this product. After reviewing Dr. Saul Kit's U. S. Patent No. 4,514,497, which describes the preparation of this modified live pseudorabies virus, we have no question that it was developed by employing recombinant DNA procedures (see "Detailed Description of the Invention," columns 10 through 14).

We, therefore, suggest that in order to avoid any misunderstanding proper State officials in any State where field trials or experimental work is being conducted should be made aware of the characteristics of this product. We are advising Veterinary Services and the Animal and Plant Health Inspection Service's Administrator that we are in the process of licensing a recombinant derived modified live pseudorabies vaccine.

Sincerely,

G. P. Shibley

George P. Shibley, Ph.D.
Chief Staff Microbiologist
Veterinary Biologics Staff
Veterinary Services

cc:
NVSL, Ames, IA (w/cy of incom)
VBFO, VS, Ames, IA (w/cy of incom)
Acting Director, VS, Scotia, NY

APHIS:VS:GPShibley:mem:436-8674:11-4-85:mll

United States Department of Agriculture | Office of the General Counsel | Washington, D.C. 20250

JUN 25 1986

APPENDIX G

MEMORANDUM

TO: Alan Tracy
Acting Assistant Secretary
Marketing and Inspection Services

FROM: John Golden
Associate General Counsel

SUBJECT: Authority to Regulate Genetically Engineered Plants Pursuant to the Federal Plant Pest Act when their Plant Pest Status is unknown.

At a hearing on June 5, 1986, Mr. James H. Scheuer, Chairman of the Subcommittee on Natural Resources, Agriculture Research and Environment, of the House Committee on Science and Technology, asked you whether the Department had statutory authority to regulate genetically engineered plants when the plant pest status of such plants was unknown. You responded that the Federal Plant Pest Act (FPPA) (7 U.S.C. §§ 150aa et seq.) provided authority to regulate such genetically engineered plants, and added that proposed regulations covering such genetically engineered plants had been drafted by the Department and were awaiting publication. The Chairman requested a legal analysis of the Department's authority, pursuant to the FPPA, to regulate such genetically engineered plants. This memorandum responds to your subsequent request for our opinion as to the Department's authority to regulate genetically engineered plants, pursuant to the FPPA , when the plant pest status of such plants is unknown.

The judicial system has "long recognized that considerable weight should be accorded to an executive department's construction of a statutory scheme it is entrusted to administer." Chevron U.S.A. v. Natural Resources Defense Council, 467 U.S. 837, 843 (1984); Aluminum Co. of America v. Central Lincoln Peoples Util. Dist., 467 U.S. 380, (1984); Blum v. Bacon, 457 U.S. 132, 141 (1982). "When a court reviews an agency's construction of the statute which it administers, it is confronted with two questions. First, always, is the question whether Congress has directly spoken to the precise question at issue . . . If, however, the court determines Congress has not directly addressed the precise question at issue, the court does not simply impose its own construction on the statute . . . as would be necessary in the absence of an administrative interpretation. Rather, if the statute is silent or ambiguous with respect to the specific issue, the question for the court is whether the agency's answer is based on a permissible construction of the statute." Chevron v. NRDC, 467 U.S. at 842-843. The Department's construction need not be the only permissible construction or even the conclusion a review court would have reached. FEC v. Democratic Senatorial Campaign Comm., 454 U.S. 27, 39 (1981).

After review of the FPPA and its legislative history, we have concluded that the language of the Act and its legislative history allow the regulation of genetically engineered plants pursuant to the Act, when the plant pest status is unknown. That review and discussions with your staff about the rationale for regulating such genetically engineered plants convince us that the Department's interpretation is consistent with the legislative intent of the FPPA and is a reasonable construction of the Department's statutory responsibilities under that Act. The Department's construction is sufficiently rational to preclude a court from substituting its judgment for that of the Department's. Young v. Community Nutrition Institute, No. 85-664, slip. op. at 7 (Sup. Ct. June 17, 1986).

The FPPA was enacted to fill gaps in the Department's authority to protect American agriculture against invasion by foreign plant pests and diseases. It confers very broad authority on the Secretary of Agriculture to prevent the dissemination into the United States or interstate of plant pests. Section 103 the FPPA provides that:

> (a) No person shall knowingly move any plant pest from a foreign country into or through the United States, or interstate, or knowingly accept delivery of any plant pest moving from any foreign country into or through the United States, or interstate, unless such movement is authorized under general or specific permit from the Secretary and is made in accordance with such conditions as the Secretary may prescribe in the permit and in such regulations as he may promulgate under this section to prevent the dissemination into the United States, or interstate, of plant pests. (7 U.S.C. § 150bb(a)).

"Plant pest," is defined as any living stage of any insects, mites, nematodes, slugs, snails, protozoa, or other invertebrate animals, bacteria, fungi, or parasitic plants or reproductive parts thereof, viruses, or any organisms similar to or allied with any of the foregoing, or any infectious substances, which can directly or indirectly injure or cause disease or damage in any plants or parts thereof, or any processed, manufactured, or other products of plants. (7 U.S.C. § 150aa(c)) (emphasis added).

Although this "can injure" language could be read to limit the authority of the Department under the FPPA to regulate only organisms which the Department has already determined are harmful to plants, in our opinion this narrow reading would fail to take into account the broad definition of "plant pest" and the clear congressional intent in enacting the FPPA to fill a gap in previously existing law. H. Rep. No. 289, 85th Cong. 1st Sess. 2 (1957).

The House report stated:

> The purpose of ... the bill is to fill a gap which has existed for a number of years in the authority of the Department of Agriculture to protect American agriculture against invasion by foreign plant pests and diseases ... under existing law the Department has the authority to regulate the importation or the interstate movement of any insects in a live state which are notoriously injurious to cultivated crops. Id. at 2 (emphasis added).

Further, the House Report, under a section entitled "Additional Authority Needed," explained that, in addition to providing authority to regulate organisms that "can injure" plant or plant products, the FPPA provides authority to regulate organisms that might later be found to be injurious to cultivated crops. In this regard, the House Report stated that Department authorities existing before enactment of the FPPA:

> ... do not provide authority to regulate the movement into or through the United States of insects that might later be found to be injurious to cultivated crops, or of mites, nematodes, protozoa, bacteria, fungi, parasitic plants or reproductive parts thereof, and viruses, which can injure or cause disease or damage in plants or their products. Id. at 3 (emphasis added).

The House Report states that the FPPA was enacted (1) to correct deficiencies in the Insect Pest Act (repealed), the Plant Quarantine Act (7 U.S.C. §§ 151 et seq.), The Mexican Border Act (7 U.S.C. § 149), and the Mollusk Act (repealed); and (2) to protect American agriculture against invasion by foreign plant pests and diseases, which, in the language of the FPPA, are "new to or not theretofore known to be widely prevalent or distributed within and throughout the United States." Id. at 3 and 9. The FPPA authorizes the issuance of regulations to prevent the dissemination into the United States or interstate of plant pests, in any situtation in which such regulations are not authorized under the Plant Quarantine Act. (7 U.S.C. § 150ee).

The proposed regulations for genetically engineered organisms are structured to prevent the release into the environment of genetically engineered organisms which are plant pests or which there is reason to believe are plant pests. The Department believes that the release of such genetically engineered organisms into the environment, is tantamount to the introduction of a plant pest which is "new to and not theretofore known to be widely prevalent or distributed within and throughout the United States." It is necessary to regulate such releases to prevent the dissemination into the United States or interstate of plant pests.

The FPPA was envisioned by American nurserymen as the statute which would create a "first line of defense" at the border and the ports of entry. Plant Pests, Control and Eradication, 1957: Hearing on H.R. 3476 Before the Subcomm. on Research and Extension of the House Comm. on Agriculture, 85th Cong., 1st Sess. 29 (1957) (statement of Richard P. White, Vice-President Am. Assoc. of Nurserymen). The Department has incorporated this "first line of defense" philosophy into its proposed regulations for genetically engineered organisms. The Department interprets the FPPA as mandating those measures necessary to prevent the introduction or dissemination of plant pests. It is within the Department's power to formulate policy and make rules to fill any gap left, implicitly or explicitly by Congress. Chevron v. NRDC, 467 U.S. at 843; Morton v. King, 415 U.S. 199, 231 (1974).

The Department has determined it is necessary to regulate unclassified or unknown organisms in order to prevent the introduction or dissemination of plant pests. Many types of organisms, particularly microorganisms, were unknown until recent years, including groups of fungi, bacteria, viruses, and viroids. In every group, a significant number of plant pests is now found.

Genetically engineered plants for which the plant pest status is unknown may be regulated for similar reasons. It has long been recognized that plants (nursery stock) present unique plant pest risks. On July 31, 1947, Congress amended the Plant Quarantine Act of August 20, 1912 (7 U.S.C. §§ 151 et seq.), to give the Secretary of Agriculture broad authority to prohibit entry without a permit of all nursery stock regardless of plant pest status. (7 U.S.C. § 154). This amendment also provided authority for post entry quarantine of that nursery stock permitted entry. (7 U.S.C. § 154). Congress reasoned that this added degree of protection was an important safeguard against pests which are not detectable by inspection. S. Rep. No. 102 80th Cong., 1st Sess. 3 (1947). Past experiences with Kudzu vine, the starling, the gypsy moth, and chestnut blight, coupled with the unknown potential effects of releasing into the environment genetically engineered plants for which the plant pest status is unknown support the reasonableness of the decision to regulate such genetically engineered plants.

It is clear that the potential benefits of genetically engineered plants are numerous, including increased yield, improved plant quality, nitrogen fixation, and disease resistance. See, e.g., Office of Technology Assessment, U.S. Cong., Impacts of Applied Genetics: Microorganisms, Plants, and Animals (1981). However, the novelty of genetically engineered plants and the lack of experience with them makes it more difficult to predict their impact on agriculture and the environment. See, e.g., Staff of House Subcomm. on Investigations and Oversight, Comm. on Science and Technology, 48th Cong. 2d, Sess., The Environmental Implications of Genetic Engineering (1984).

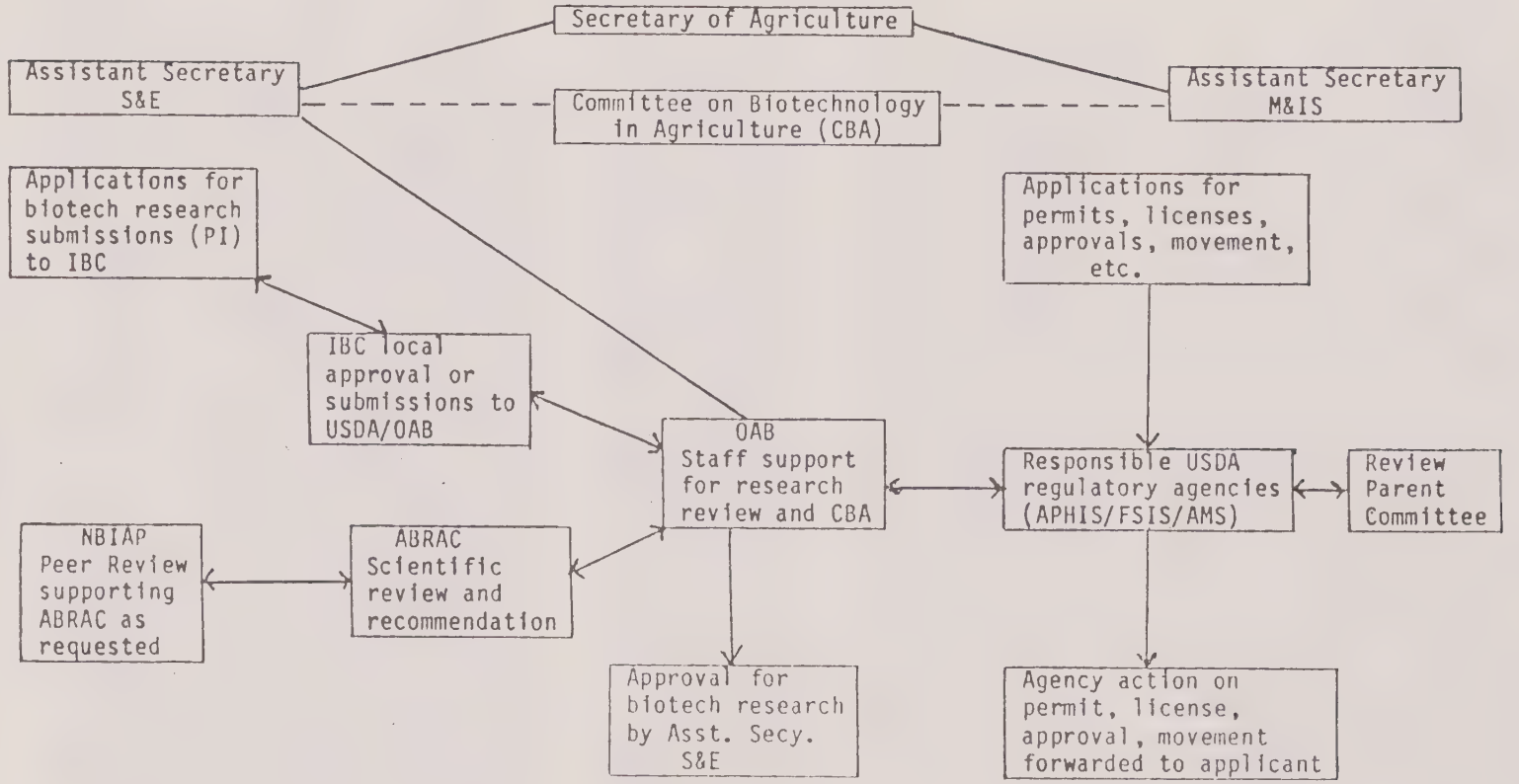
In view of these circumstances it appears that a decision not to regulate such genetically engineered plants would be contrary to the congressional intent of preventing the introduction and dissemination of organisms that "might later be found to be injurious." Plant Pests, Control and Eradication, 1957: Hearing on H.R. 3476 Before the Subcomm. on Research and Extension of the House Comm. on Agriculture, 85th Cong., 1st Sess. 15 (1957). Where the congressional intent is clear that intention is law and must be given effect. Chevron v. NRDC, 467 U.S. at 843: FEC v. Democratic Senatorial Campaign Committee 454 U.S. at 32.

"If Congress has explicitly left a gap for the agency to fill, there is express delegation of authority to the agency to elucidate a specific provision of the statute by regulation. Such ... regulations are given controlling weight unless they are arbitrary, capricious, or manifestly contrary to the statute." Chevron v. NRDC, 467 U.S. at 844; United States v. Morton 467 U.S. 822, 834 (1984). It should also be noted that the Supreme Court has held that statutes providing broad authority may be held to encompass products of new technology never envisioned by Congress when the statutes were enacted. Diamond v. Chakrabarty 497 U.S. 303, 315 (1980).

It is therefore our opinion that the Department's interpretation of the FPPA as providing the authority to regulate such genetically engineered plants and organisms is a permissible construction of the Act.

USDA
9/25/86

FLOW CHART FOR BIOTECHNOLOGY APPLICATIONS

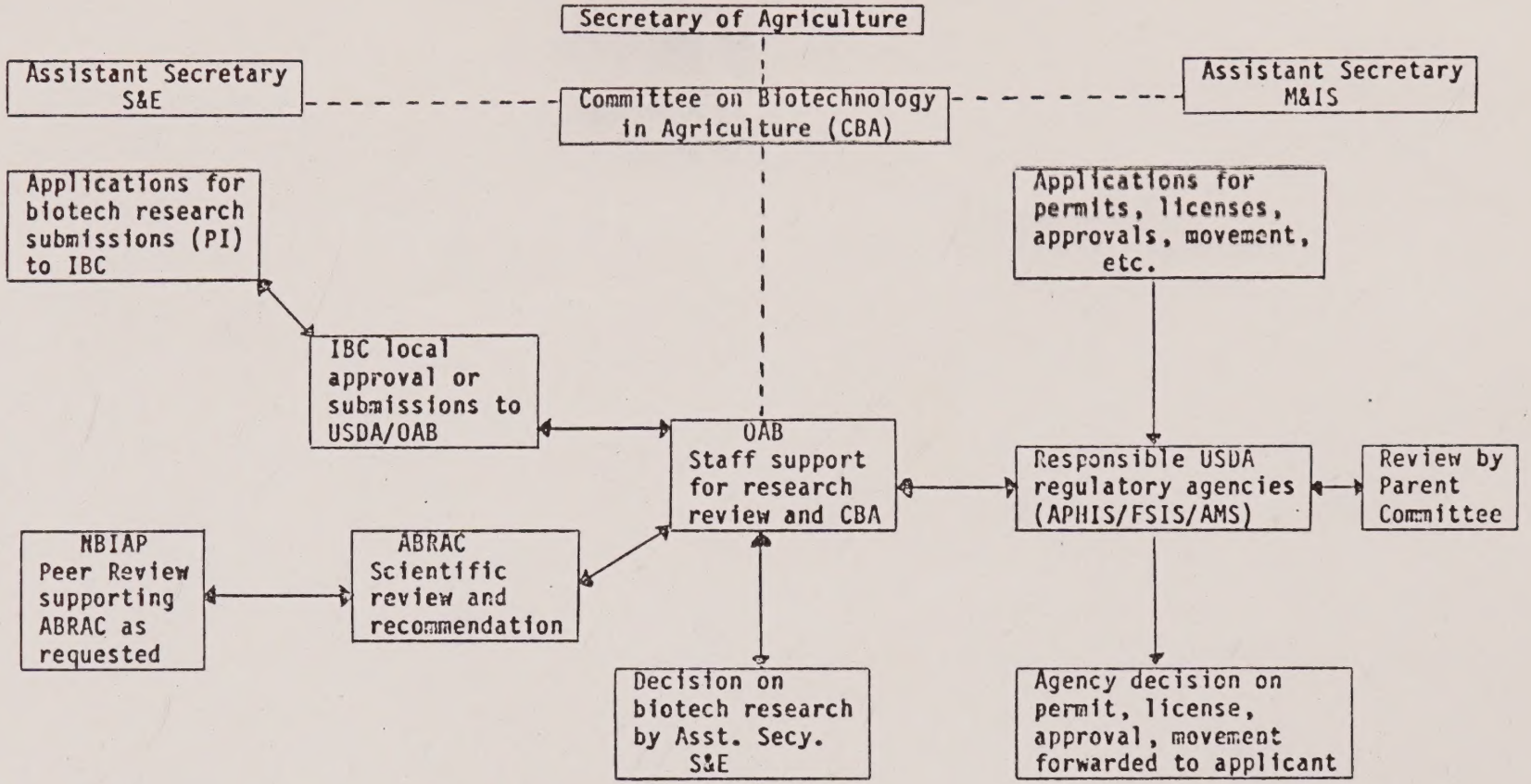


Terms:

ABRAC - Agricultural Biotechnology Recombinant DNA Advisory Committee
AMS - Agricultural Marketing Service
APHIS - Animal and Plant Health Inspection Service
CBA - Committee on Biotechnology in Agriculture
FSIS - Food Safety Inspection Service
IBC - Institutional Biosafety Committee
M&IS - Marketing and Inspection Service
NBIAB - National Biological Impact Assessment Program
PI - Principal Investigator (Research)
OAB - Office of Agricultural Biotechnology
S&E - Science and Education

10/14/86

FLOW CHART FOR BIOTECHNOLOGY APPLICATIONS



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ABRAC - Agricultural Biotechnology Recombinant DNA Advisory Committee
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PI - Principal Investigator (Research)
OAB - Office of Agricultural Biotechnology
S&E - Science and Education

JJB - 10/15/86
KAS - 10/14/86